ACUTE MEDICAL DISORDERS

Diagnosis and Treatment

By
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Foreword By
GEORGE MORRIS PIERSOL, M D

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This book

is affectionately dedicated

to

ANTHONY F BERENS, S J

Foreword

THE acute episodes of disease and the emergencies which at times attain life endangering importance must be regarded as among the most disturbing problems that confront the practitioner of medicine The recognition of this fact led Dr Murphy to undertake the preparation of a volume which is unique in that it is devoted entirely to the diagnosis and treatment of those acute conditions which ordinarily come under the observation of the internist and general practitioner

Few men are so well qualified to write such a book as is Dr Murphy By reason of his long years of service in the practice of internal medicine and in the medical wards of large general hospitals he has been able to embody in his writings observations and suggestions that not only represent much careful study but which are based primarily on an extensive practical clinical experience

The subjects which are discussed in his book have been selected because over the years the author has found them to be the acute conditions with which he has been most frequently confronted When a physician is faced with some acute episode in the course of a disease he needs precise information in a concise and readily available form This volume is the only text with which we are familiar that meets these requirements and makes it possible for the hard pressed doctor to obtain urgently needed help without searching numerous comprehensive medical texts

Dr Murphy has sought to make this book essentially practical To that end long discussions of etiology and pathology have been sacrificed and diagnosis especially differential diagnosis and treatment emphasized The management of patients has been gone into with great detail so that the reader can obtain exact information as to

Preface to the Third Edition

THE warm reception given the first two editions of this book by medical students and physicians indicates that this third revision is warranted

Advances in medicine are so rapid especially in the field of therapeutics that chapters on the treatment of acute bacterial diseases with sulfonamides and antibiotics cardiac disorders and metabolic disturbances require frequent revision to be of help to the physician In making this revision the fundamental purpose of the book has been constantly kept in mind—that of giving to the general practitioner and the student of medicine a concise yet accurate discussion of some of the most important problems met with in practice Originally this book aimed at giving briefly the main clinical features of acute disorders without including unnecessary and controversial details Most important of all however it aimed at advising a physician what to do for a patient in an acute emergency and how to do it as far as is possible These aims have not been forgotten Many suggestions constructive criticisms and letters have been received since this book first appeared and they have been most helpful in bringing this edition up-to-date

As in the past this book is written with the idea of expressing my own opinions about the importance of certain diagnostic procedures and certain therapeutic measures These have been arrived at largely from personal experience at the bedside This does not mean that opinions of others are considered unimportant or that I have not made use of them in writing this edition but to do justice to the many authors consulted and the many opinions reviewed it would require a much larger volume and probably would defeat the original purpose of this book

how to carry out the suggested therapies It will be found that the acute situations with which the doctor is ordinarily confronted are all covered in this volume

Dr Murphy is to be congratulated upon having produced a work of unusual value and which reflects his own ideas and experience It should prove of especial interest not only to medical students and young physicians but also to those of ripe experience who nevertheless are only too often puzzled and disturbed by the acute and dramatic manifestations presented by most medical conditions

GEORGE MORRIS PIERSOL M D

Preface to the First Edition

THIS book is intended for the general practitioner and medical student For more than 20 years as Clinical Director of the Milwaukee County General Hospital and the Emergency Unit as a teacher and as a practitioner I have observed that while chronic illnesses are managed very satisfactorily many difficulties are encountered in the care of the acute disorders What I have put down here is the result of my experience during active medical practice It has been my belief that the basis of what one teaches should consist of facts which he has proved to his satisfaction

This book was written with the aim of passing on to the practitioner diagnostic procedures and methods of treatment which have been found helpful in the management of the acute case Acute disorders are apt to occur with dramatic suddenness and the physician when called must mobilize at once his store of general knowledge and be prepared to act quickly and with precision If one is working in a hospital fully equipped for such cases the task is hard enough but the one who is called to see the patient in the home at the factory or on the street is face to face with a critical problem that taxes his skill and judgment to the utmost and his decision may mean the life or death of the patient.

The size of this book does not warrant the inclusion of a bibliography and lengthy references but I am not unaware of the many splendid contributions which have appeared in the medical literature and the helpful suggestions I have gained from them Diagnostic and therapeutic methods have been brought together into what I believe to be a practical plan for the management of the patient If I have been successful in presenting a few useful hints in diagnosis and treat

In practically all of the chapters additions and corrections have been made, and the chapters on metabolic disorders tropical diseases and diseases of the liver have been almost completely revised and extended Those chapters which deal with penicillin and other antibiotics and sulfonamides have also been brought up to date as have the newer methods of managing the various kinds of heart diseases

Again I should like to take this occasion to express my cordial thanks to my colleagues Drs William L Coffey Jr Paul G LaBissoniere and James H Topp who have been most generous and helpful to me in making this revision I should especially like to thank Miss Grace Treutinger for her patience and skillful guidance in the preparation of the third edition

FRANCIS D MURPHY M D

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ment or have served to remind some reader of information possessed at one time but now half forgotten this book will have fulfilled its purpose

Finally I would like to express my cordial thanks to the House Staff of the Milwaukee County Hospital who have been generous and helpful to me in writing this book and especially to Miss Audrey Salb for her patience skillful help and guidance in the preparation of the manuscript

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CHAPTER I

Vascular Disease

HYPERTENSIVE CEREBRAL VASCULAR CRISIS

Hypertensive cerebral vascular crisis is a name applied to a transient attack of amnesia hemiplegia or aphasia or of some other cerebral episode which may occur in any of the stages of essential hypertension but which usually appears in the later stages of the disease It is characterized by abrupt onset short duration and sudden disappearance

This important syndrome is more properly termed the acute vascular crisis of hypertension and corresponds to the vascular crisis of Pal Other names which have been erroneously given to this syndrome are the pseudo uremia of Volhard the hypertensive encephalopathy of Oppenheim and Fishberg and the pseudotumor of Nonne The latter three are usually manifestations of malignant hypertension or secondary to the hypertension due to chronic nephritis The syndrome here described is most generally observed in patients with essential benign hypertension

Etiology Pathogenesis of this spectacular complication of hypertension is still rather vague It would appear as though the sudden onset of symptoms was brought about by an abrupt rise in blood pressure Some feel that this is due to marked spasm of the cerebral vascular system or at times may be caused by acute cerebral edema as seen in eclampsia and in acute glomerulonephritis Others have attempted to show that the arterioles are not spastic but are dilated resulting in an increased pressure in both the arterial and venous sides of the capillary network This latter phenomenon may occur in younger individuals in whom cerebral edema may be the chief factor while it is very likely that a sudden rise of blood pressure in the older age groups is due to the inability of the cerebral arterioles to relax At times a definite increase in intracranial pressure is reflected in an increased spinal fluid

Pathology Histologically examination of the brain fails to reveal vascular changes This would tend to support the spasm theory or

1 The patient should be kept in a comfortable position

2 Spinal tap and slow drainage of fluid is indicated if pressure is high

3 Fifty to 100 cc of 50 per cent sucrose or glucose may be given intravenously twice a day

4 Vasodilators such as nitroglycerin amyl nitrite and xanthine derivatives may be of value

5 Papaverine hydrochloride 0 3 Gm (1/5 grain) intravenously every 3 hours or 0 9 Gm (1 1/2 grains) orally four times a day when the patient is able to swallow may prevent the attacks This drug has been found effective in decreasing the severity and frequency of seizures even in patients with advanced malignant hypertension

6 Hormonal therapy has been tried with some success Testosterone propionate may be given intramuscularly to males The dosage is four 25 mg (5/12 grain) injections in the first week three injections of 25 mg (5/12 grain) in the second week 10 mg (1/6 grain) doses three times a week for the next two weeks 10 mg (1/6 grain) twice a week for the next three weeks and 10 mg (1/6 grain) once a week up to the twelfth week of therapy Females are given mixed estrogens and estrones in 10 000 I U doses and estradiol dipropionate in doses of 0 2 mg (1/300 grain) Four injections are given in the first week three injections a week are given for the next four weeks two a week for the following four weeks and one for another four weeks This therapy has been said to reduce blood pressure improve cerebral circulation and reduce the symptoms of hypertensive encephalopathy

DISSECTING ANEURYSM

A dissecting aneurysm is an extravasation of blood within the wall of a blood vessel as a result of rupture of the intima While such an aneurysm of the aorta was first described in 1728 by Nicholls it was not until 1819 that the term dissecting aneurysm was originally employed by Laennec In 1856 Swaine was the first to make a correct ante mortem diagnosis of the condition but until 1934 when Shennan published his monograph of 300 cases the disease was diagnosed uncommonly Today however because of a better acquaintance with the symptomatology the diagnosis is made in 10 to 30 per cent of cases

the theory of altered arterial or arteriolar response to an increased blood pressure. *Some cases reveal cerebral edema which may also be* explained on the aforementioned basis. There is not much doubt that spasm may be the etiological factor in younger patients but the physiological vascular response theory is more applicable to the older patients.

Signs and Symptoms. Clinical evidence of what appears at first to be a cerebral hemorrhage sets in abruptly. In some cases there is complete hemiplegia in others only a cloudiness of mentality develops which gradually increases until the patient is in the twilight zone of consciousness. The symptom complex in its milder form is characterized by an increasingly severe headache mental confusion and drowsiness. This is followed by dizziness nausea vomiting and visual disturbances. The more severe cases may develop temporary aphasia paresis paralysis convulsions and even coma. Usually the symptoms subside as rapidly as they appeared. It is not uncommon to see a patient with a complete paralysis of one side of the face the leg and arm only to find several hours later that there is no evidence of paralysis or even a residual paresis. The attacks occur in two definite types of patients (1) Those with evidence of cerebral edema who are usually under 40 years of age and (2) those without evidence of cerebral edema usually over the age of 40.

My own observations of *this disorder prompt me to emphasize* the importance of keeping an open mind when a hypertensive's behavior verges on the pathological side. Sometimes such patients appear drunk mentally disordered or merely vicious and reckless. Final diagnosis should be made slowly and carefully remember things are not always what they appear to be on the surface.

Prognosis. Prognosis does not depend on the acute vascular attack but rather on the changes that occur in other vital organs in association with the crisis the most salient of which are the heart and kidney. Recovery is usually prompt and spontaneous and thereby the prognosis differs from that of true cerebral hemorrhage thrombosis or embolism.

TREATMENT

In general masterful inactivity is the therapy of choice. An ice bag applied to the head and a hot water bottle to the feet are usually sufficient but the following may be *instituted*

and lumbar arteries Patchy and bizarre neurological findings may ensue Rupture of the aneurysm back into the main channel of the aorta may permit recovery to occur with the formation of a so-called double barreled aorta The wall of the aneurysmal vessel may rupture into the pericardium mediastinum pleural cavities or further downward

Signs and Symptoms The most striking symptom produced in this condition is excruciating pain followed by collapse or sudden unconsciousness The location of the pain varies with the site of the aneurysm but characteristically it exhibits a migratory tendency It may begin in the precordium or in the epigastrium pass to the neck or jaw and later to the back flanks and legs or any one of these areas may be involved Radiation of the pain to the arms is less common than in myocardial infarction Occasionally the pain may disappear only to return again at some later date Many patients have been labeled as neurotics until subsequent and more severe episodes give convincing evidence of dissecting aneurysm The pain is usually accompanied by pallor sweating prostration and often by loss of consciousness Coma is especially likely to occur if the carotid arteries are involved in the dissection In the latter case hemiplegia or other manifestations of central nervous involvement may supervene The development of neurological signs from ischemia of the spinal cord greatly facilitates the diagnosis There should be a search of both motor and sensory changes they may be transitory but are characteristically segmental in distribution Peripheral neuritis may develop Fever may be present and vary widely in degree

When rupture of the intima occurs in the descending thoracic or abdominal aorta confusion with renal or other abdominal disease is likely and external rupture in this situation may produce extensive extravasation of blood If such extravasation is detected externally the acute surgical abdomen may be suspected Clinical features which may be present at this time are jaundice cyanosis and engorgement of the thoracic veins inequality of the blood pressure from one extremity to the other left recurrent laryngeal paralysis dysphagia and dyspnea Left sided pleural effusion or atelectasis of the left lower lobe may occur and hematuria and at times anuria are seen Arterial pulsation may be lost in one or more extremities even upon palpation

Etiology and Pathology The frequency of dissecting aneurysm although varying somewhat from report to report ranges between 1 in 200 to 1 in 552 cases and an average of these figures places the incidence at 1 in 376 cases It is reported that approximately three fourths of cases occur in males between the ages of 40 and 70 years Antecedent hypertension or cystic medial necrosis is the usual cause syphilis trauma and exertion are infrequent etiological agents In patients under 40 with this condition hypertension is present in only half of the cases the basic lesion being a degenerative cystic necrosis of the media Occasionally a congenital narrowing of the aorta is present in these individuals

A dissecting aneurysm usually involving the aorta results from rupture of the intimal lining of any large blood vessel An arteriosclerotic plaque or a point of rupture of one of the vasa vasorum is the main site of origin The lesion is associated with arteriosclerotic changes in the elastic tissue of the medial coat of the vessel and degeneration of the media leads to changes in the wall which pave the way for dissection by the aneurysm Blood from the lumen is forced through the tear in the intima into the medial coat where dissection begins at once and progresses very rapidly depending on the height of the systolic blood pressure and the degree of degeneration of the medial elastic tissue The sudden rupture of the intima and tearing of the media allows the blood to dissect its way between the layers along the entire course of the aorta or through the media of the subclavian arteries or the iliac arteries This extravasation of blood under high pressure is thought to be precipitated by emotional excitement or sudden physical exertion

Impairment of the circulation to and from adjacent viscera results in variable pathology There may be pressure on the thoracic veins by the aneurysm interference with the cerebal circulation because of involvement of the carotid or innominate arteries or pressure on the esophagus or on the left recurrent laryngeal nerve Compression of the left lung is also fairly frequent and at times partial occlusion of the renal arteries is seen Embarrassment of the peripheral circulation in the extremities results from further dissection of the aneurysm downward resulting in gangrene or less severe peripheral vascular changes Also evidenced may be degenerative changes within the spinal cord due to an interruption of the blood flow in the intercostal

ACUTE THROMBOPHLEBITIS AND PHLEBOTHROMBOSIS

Acute thrombophlebitis and phlebothrombosis have long been the bane of the surgeon as well as of the physician They complicate from one to two per cent of surgical procedures and a number of cases are encountered during or following medical disorders including heart disease infection with secondary vein involvement varicose veins and blood dyscrasias They are important not only because they are in themselves capable of causing pain and disability but also because they are the precursors of pulmonary embolism with all its tragic complications The prophylactic and active treatment of thrombophlebitis and phlebothrombosis go far in reducing the incidence of pulmonary embolism

Etiology and Pathology The initial cause of thrombophlebitis is believed to be a diseased vein itself and infection and varicosities are strong factors in its development For some reason the intimal lining becomes injured either by toxins irritants or bacteria and particularly when the venous blood flow is slow there is a tendency for a thrombus to form within the injured veins because the blood platelets adhere very readily to the intimal lining These agglutinated platelets act as a center for the building up of the fibrin clot This process is encouraged by sluggish venous blood flow and an increase in both the blood platelets and the blood fibrinogen Boyd explains *the changes in the vascular endothelium and says they usually cause* the clot to be firmly attached to the vessel wall so that there is little danger of its becoming detached If the infection is septic the thrombus tends to become softened and to disintegrate

The term phlebothrombosis is reserved for that type of intravenous thrombosis which occurs rather suddenly and produces very few clinical signs This is the form which is usually seen postoperatively and which gives rise to most of the massive fatal pulmonary emboli Phlebothrombosis results from the interaction of a number of factors the most important of which arise from changes which go on in the blood to increase its coagulation power It has been known for some time that patients who are anemic and who have an elevated plasma fibrinogen together with increased numbers of blood platelets are prone to develop a pulmonary embolism All of these facts together with a slow venous circulation time in the veins of the lower

of the abdominal aorta Progressive failure of motor power in the lower extremities may also be evidenced The legs become cold cyanotic and flaccid and gangrene may be a terminal episode In the majority of patients the blood pressure remains elevated throughout the disease even in the presence of a syndrome that otherwise resembles shock Pain may be remarkably absent in the clinical picture even when the dissection is extensive although at times vomiting may be associated with epigastric pain

Diagnosis Characteristic electrocardiographic findings *show no* distinct or diagnostic pattern in dissecting aneurysm but will distinguish it from coronary occlusion *which presents no distinctive* EKG changes Unilateral hematuria is significant if it originates in the side in which the neurological lesions are most extensive Roentgen examination of the chest frequently shows definite widening of the aorta and aortic pulsations are often diminished Cardiac hypertrophy may be present and the trachea and esophagus are frequently displaced Roentgen examination of the abdomen may by the presence or absence of free air under the diaphragm aid in differentiating dissecting aneurysm from a ruptured abdominal viscus

Prognosis Dissecting aneurysm of the aorta is a common cause of sudden death The prognosis is poor and 80 per cent of patients die within the first day or two Patients who do recover should have their activity markedly restricted

TREATMENT

1 Absolute rest should be enforced with opiates and barbiturates

2 Oxygen may be used to relieve dyspnea and restlessness

3 External heat may be advisable

4 Nitrites are recommended for lowering the blood pressure and thus decreasing the degree of dissection For the latter purpose venesection *has also been advised but vasodilators are preferable*

5 Surgery to reunite the cavity of the aneurysm with the main channel of the aorta has been conceived and attempted but a successful *outcome must* necessarily presuppose very accurate diagnosis the best of surgical skill and a happy combination of circumstances

TREATMENT

The treatment of thrombophlebitis consists of rest and quiet for the involved extremity and heat given either in the form of moist dressings diathermy or a cradle heated by electric lights This results in relaxation of both the venous and arterial trees to a remarkable degree Vasodilating procedures should be started and the limb should be elevated to a level of 6 inches above the heart especially when edema is present so as to drain the lymph and venous stasis fluid from the extremity Fluids and salt should be restricted in the diet salyrgan 1 to 2 cc may be given intravenously every other day for three doses and it is advisable to give ammonium chloride 1 Gm (15 grains) three times a day By this intake of fluid dehydration may be avoided since it tends to increase the thrombosing tendency Thyroid extract by mouth has also been recommended Deep breathing is to be avoided because it returns blood to the heart and may introduce negative phases of pressure which tend to break any loose thrombi

Heparin which was discovered by Howell and MacLean and later purified and made available for clinical use is the physiological anticoagulant The average dose is 50 mg four times daily increased or decreased to maintain a clotting time of 20 to 30 minutes Apparently its natural force in the living organism is the granules of tissue mast cells These granules together with the granules of the blood basophiles react to the same chemical tests as heparin Heparin is most likely an antiprothrombin and an antithrombin It also inhibits the agglutination of the blood platelets When heparin is given intravenously it prolongs both the coagulation time and the clot retraction time and Hirschboeck and Coffey have pointed out that when the clot retraction time is short (below 10 minutes) the patient may be considered to be a possible candidate for pulmonary embolism They then advise prophylatic treatment with heparin

Another anticoagulant dicumarol the synthetic toxic agent of spoiled sweet clover is equally satisfactory It is cheaper may be given orally and has a prolonged effect Its action is however slower than that of heparin Three hundred mg of dicumarol is given on the first day and 200 mg the second day and each succeeding day when prothrombin is less than 20 per cent or until the possibility of pulmonary emboli no longer exists For a continuous effect one of

extremities predispose toward the development of a loose noninflammatory thrombus within the vein *Because of the high fibrin content* and the strong retracting power of these thrombi it is easy for them to become dislodged Pulmonary emboli may of course arise from thrombophlebitis but it is in phlebothrombosis *that most cases of* pulmonary embolism are evidenced

Signs and Symptoms The superficial veins of the lower extremity are most frequently involved Once the thrombosis has occurred the *vein becomes cordlike and tender* The skin and tissues about the vein are reddened and the features of an inflammatory reaction are present The thrombophlebitis is frequently introduced by a rather sharp pain in the lower extremity itself or in the groin and the leg may become swollen to twice its normal size particularly when the deep femoral tributaries are affected After the extremity becomes swollen which usually occurs within a few hours or a day or so one is able to palpate tender areas along the course of one of the larger venous tributaries One can elicit pain in the calf and plantar region if there is a thrombosis of the smaller veins in these regions by exerting pressure with the hands If the thrombophlebitis is superficial we may notice a reddened warm area of inflammatory reaction along the course of the diseased vein When the process is generalized in the main veins of the extremity the swelling may become quite extensive and the condition is then called phlegmasia alba dolens

Clinically it is seen that attempts to bear weight on the extremity causes considerable pain to the patient There is also a frequent elevation of temperature accompanied by an occasional chill

Prophylaxis In the past there has been too much emphasis upon diagnosis and treatment and too little on prevention No factor which contributes to the efficient circulation of blood in the extremities can be overlooked in the prevention *of clot formation In bedridden* patients deep breathing exercises active bed exercises and shortened postoperative bed rest are advocated as prophylactic measures In addition a study *of each patient is necessary to determine* if he has a history of thrombophlebitis or phlebothrombosis or and this is equally important if he has a tendency to develop one of these complications because *of a physical* defect or a medical disorder All of these patients should receive prophylactic treatment with one of the anticoagulants heparin or dicumarol which will be discussed under treatment

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the best methods of treatment is to administer both drugs simultaneously and then to discontinue the heparin after 48 hours

Determinations of prothrombin and coagulation time are made daily during anticoagulant therapy If an excessive prothrombin deficiency occurs the anticoagulant is discontinued and menadione bisulfite (synthetic vitamin K) 60 to 64 mg is administered intravenously The risk of hemorrhage must be kept in mind it can be controlled by transfusions of serum or whole blood and by intravenous administration of menadione bisulfite

Dicumarol alone may be administered prophylactically or therapeutically in many cases with complete success However it cannot replace quick acting heparin in emergencies and neither of these drugs can be considered alternatives to indicated surgical procedures Heparin and dicumarol cannot dissolve a blood clot once it has formed their usefulness lies in prevention of clot formation

There are several contraindications to the use of anticoagulants (1) A renal or an hepatic insufficiency (2) subacute bacterial *endocarditis* (3) *blood dyscrasias* (4) *purpura* (5) *recent* operations particularly on brain or spinal cord In addition great care must be taken in administering these drugs to patients who have (1) Open wounds or ulcerative lesions (2) gastric or intestinal obstruction or drainage (3) nutritional deficiency

The treatment of phlebothrombosis is essentially the same as for thrombophlebitis Bed rest is imperative in order to prevent a dislodging of the clot However some advocate the use of tight bandages to the extremity and active or passive exercise in the management of both phlebothrombosis and thrombophlebitis Paravertebral nerve block is advised by many surgeons It is considered wise to remove any foci of infection especially fungous infections sulfonimide arsenic and bismuth therapy may be used for this purpose Recently there have been reports of excellent results following ultraviolet blood irradiation therapy Massage baths exercise and vitamin B may be instituted to combat the neuritis when the process is healed Recently Baily has pointed out that femoral thrombectomy is indicated in patients with phlebothrombosis when pulmonary embolism has occurred and the patient is yet in a condition to withstand operation

In acute cases of thrombophlebitis and phlebothrombosis and in cases where anticoagulants are *contraindicated surgical ligation*

of the appropriate vein above the level of the thrombus may be necessary Risks of ligation are few postoperative complications are absent except for an occasional transitory increase in edema Many physicians consider ligation the most direct and practical method of preventing pulmonary embolism and restoring normal circulation

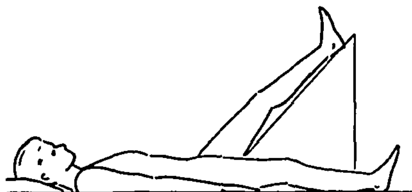


Fig 1—Acute occlusion in the peripheral arteries The wrong position of leg when there is an acute arterial obstruction

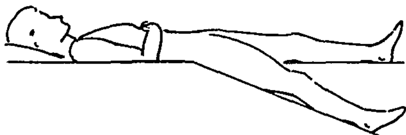


Fig 2—Acute occlusion in the peripheral arteries The correct position of leg when there is an acute arterial obstruction

ACUTE OCCLUSION IN THE PERIPHERAL ARTERIES

Acute vascular occlusion may occur in an individual whose peripheral vascular tree is normal but more frequently develops in a patient who has had some disease of the peripheral arteries as arteriosclerosis These acute episodes may be classified as follows

1 Embolic occlusions frequently seen in patients with heart disease

the best methods of treatment is to administer both drugs simultaneously and then to discontinue the heparin after 48 hours

Determinations of prothrombin and coagulation time are made daily during anticoagulant therapy If an excessive prothrombin deficiency occurs the anticoagulant is discontinued and menadione bisulfite (synthetic vitamin K) 60 to 64 mg is administered intravenously The risk of hemorrhage must be kept in mind it can be controlled by transfusions of serum or whole blood and by intravenous administration of menadione bisulfite

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In acute cases of thrombophlebitis and phlebothrombosis and in cases where anticoagulants are contraindicated surgical ligation

3 The underlying disease must be recognized and treated accordingly

1 Improving the blood supply to the extremity

a The extremity must not be elevated but should be lowered in order to augment the blood flow into the obstructed area

b Heat is essential but must not be too great otherwise blisters may form and more harm than good done Most patients do best with 32 2 to 36 7 C (90 to 98 F) *Heat higher than body temperature is contraindicated*

c Passive exercises may be helpful

d Codeine and papaverine may be given intravenously in 32 mg (1/ grain) doses two or three times a day or 0 6 mg (1/100 grain) atropine sulfate may be given they help dilate the spastic smooth muscles and augment the blood flow to the diseased extremity

e Intravenous injections of 200 cc of five per cent sodium chloride or sodium citrate solution every day helps at times

f Massage is not indicated in the acute phase After a few days light massage may be helpful

g Passive vascular exercise with the suction machine is of great benefit, especially in acute embolic occlusion Pavex is not so useful in arteriosclerotic disease or in Buerger s disease

h Intermittent venous hyperemia is a system of treatment which is based on compression of the return venous flow followed by release of compression This method of treatment is satisfactory in chronic conditions but not very helpful in acute occlusions

i Surgical treatment as paravertebral block of the sympathetic nerve chain is indicated in all cases of acute arterial occlusion to interrupt the reflex vascular spasm increase the blood flow through the collaterals and thus check the formation of descending thrombosis distal to the embolus It should also be done before all embolectomies and after all arterial ligatures

j Clot should be removed by embolectomy if less than ten hours have elapsed since the occurrence of the massive obstruction if the general circulation is fairly well maintained and if there is no severe peripheral arteriosclerosis If the patient has been conservatively treated within the first ten hours without improvement in his condition embolectomy should be performed

k Heparin and heparin like substances have been used but their main role is in the prevention of the thrombosis which occludes the arteries rather than in treatment after occlusion has occurred Doses of from 30 to 50 mg every 4 hours is given intravenously Dicumarol is started at the same time giving 300 mg to begin and 200 mg daily if the prothrombin is over 20 per cent of normal The heparin is discontinued when the prothrombin time is 30 per cent or less

2 Arteriosclerosis followed by thrombosis arteritis or injury
3 Thromboangiitis obliterans
4 Syphilitic arteritis

Chronic diseases of the peripheral arteries as arteriosclerosis arteritis and thromboangiitis obliterans are comparatively common and their treatment is well understood The sudden occlusion of a peripheral artery as it occurs in a patient with auricular fibrillation or in thromboangiitis obliterans or in an arteriosclerotic person constitutes an acute emergency of great importance While it is important to determine the exact kind of pathological lesion causing *the obstruction to the circulation it is far more important to realize* that the reestablishment of an adequate blood supply to the involved limb is of much greater concern The outstanding fact to be remembered is that the blood supply has been cut off whether the lesion is embolic arteriosclerotic or thrombotic may be determined at a later date

Signs and Symptoms The symptoms that occur with sudden arterial occlusion are pain paleness of the extremity coldness and numbness Pain and coldness are the chief symptoms and the main indicators of response to treatment

The involved limb must be handled gently as the pain is frequently almost shocking in character Inspection reveals marked pallor elevation of the limb accentuates the pallor while lowering of it frequently causes redness Palpation reveals not only coldness but lack of pulsation in the dorsal pedis and posterior tibial When there is a venous involvement as in thromboangiitis obliterans the vascular system of the extremity is overfilled and the foot is puffy and apt to be purple not pale as in pure arterial occlusion

Diagnosis The diagnosis of acute occlusion is not at all difficult though the underlying disease may be hard to recognize It is obvious that in acute vascular occlusion there is a certain degree of vascular *spasm which develops in association with the organic plug*ging of the vessel In treatment both conditions must be considered at the same time

TREATMENT

1 The blood flow to the involved extremity must be improved
2 Pain must be relieved

in shock are featured by capillary and venous congestion involving particularly the internal organs Congestion is not caused by obstruction to the return flow of blood to the heart but by dilatation of the capillaries The term acute venous congestion is used to indicate the changes present at autopsy As yet there is no complete agreement as to the mechanism of production of these pathological

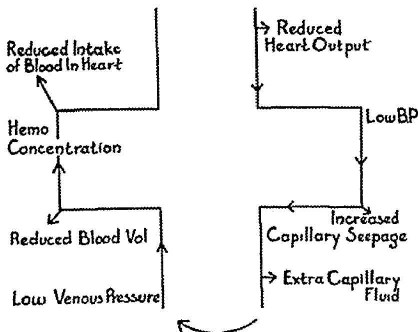


Fig 3—Shock Diagram showing sequence of events in shock

changes but the visceral engorgement that is always present regardless of the primary cause in shock is probably not the result of any one factor but a combination of conditions Atony and dilatation of the capillaries cause increased permeability and seeping of fluid into the tissue spaces This leads to diminished blood volume and reduced return flow of blood to the heart a decreased cardiac output and hemoconcentration (see diagram) Associated changes of many kinds may be present such as alterations in the electrolyte pattern deficiency of adrenal cortical substance and changes in the nerve cells of the brain and the peripheral nervous system but these are more apt to be results than participants in the main pathological event

1 Repeated intravenous injections of typhoid vaccine are said to be helpful in some cases but in patients with coronary disease chronic heart disease or any debilitating disorder these vaccines are contra indicated

2 The relief of pain in the acute phase requires morphine 30 mg (½ grain) at once plus 15 mg (¼ grain) in half an hour papaverine 0 2 Gm (3 grains) every three hours codeine 60 mg (1 grain) or demerol 200 to 300 mg Papaverine and codeine are the drugs of choice It is unwise to continue the use of these narcotics *after the acute phase is over because of the possibility of the patient* becoming addicted to the drug Luminal seconal or bromides had better be substituted for the narcotics after the first several days *Nerve block* or parasympathectomy may have to be resorted to for relief of pain at times

3 If auricular fibrillation or some other form of heart disease is the cause of the embolus attention must be directed to the underlying disease

SHOCK

There is no unanimity of opinion over the definition of the term shock and the loose manner in which the term has been commonly *employed has contributed to the confusion* in nomenclature Attempts to classify it by adding a number of adjectives as neurogenic hematogenic toxic primary secondary and so forth have not lessened *the confusion For practical purposes* shock may be defined as an acute circulatory deficiency characterized by oligemia decreased cardiac output and hemoconcentration Certain common disorders such as *heart failure pneumonia hypertensive carotid sinus* disorders and many infectious diseases may cause signs and symptoms which closely simulate shock and their differentiation from shock is particularly *important from the standpoint* of therapeutics

Etiology Injuries burns infections as pneumonia and abdominal operations and emergencies as volvulus mesenteric thrombosis pancreatitis play a *prominent* rôle in the cause of shock Obviously a variety of other conditions may be responsible for the disorder

Pathology Within recent years painstaking investigations have shown that shock *is a definite* entity and that characteristic clinical and postmortem changes are demonstrable The pathological changes

lation exists between the degree of shock and the extent of biochemical changes These changes include hyperglycemia lactacidemia a fall in the bicarbonate reserve and a reduction in the oxygen saturation of the blood An elevation of the alpha amino nitrogen of the blood plasma a lengthening of the prothrombin time and an elevation of the icterus index are common

Diagnosis Heart failure especially the acute kind hemorrhage and shock are confused with one another As far as hemorrhage is concerned some believe the differentiation from shock is an unnecessary mental exercise however certain points in differential diagnosis will be pointed out.

Heart failure presents a picture of failing circulation characterized by pulmonary congestion engorgement of the liver kidneys *spleen* and intestines and of most importance the large veins of the superficial type are engorged A failing heart is enlarged from hypertrophy and dilatation and it is usually irregular As a rule some evidence of an etiological factor in heart disease is present as hypertension coronary disease valvular leakages or hyperthyroidism When the state of shock sets in the circulatory deficiency is neither cardiac nor vasomotor in origin and while some features of cardiac collapse may be present certain clinical features characterize shock The large veins of the neck as well as the superficial veins in other parts of the body are collapsed and empty The heart is usually very rapid and regular Enlargement of the heart as seen in heart disease *is characteristically lacking in shock and while the blood pressure* may be reduced to a very low point in heart failure in shock it is extremely low or imperceptible And finally in shock the valvular leakages and other disorders that may cause heart failure are lacking

In days gone by the lack of differentiation between shock and heart failure in pneumonia constituted an important error which led to a mistaken idea of therapy The rapid regular heart with the *thin thready pulse cold clammy skin and ashy* cyanotic tinge was for a long time considered the toxic effect of pneumonia upon the heart *itself* Digitalis and other cardiac stimulants were used almost universally sometimes in large doses to control the so-called heart failure However subsequent studies of the shock *syndrome revealed* that in pneumonia it was not the heart as a rule that was at fault but rather that the chief trouble was in the periphery in the capil

Signs and Symptoms The shock syndrome need not have all of the diagnostic features present at the beginning for there are characteristic features which come in the earlier phases of shock and others which develop later For our present purpose all will be discussed together Vomiting pallor and a cold clammy skin are the main features in nearly every case The pulse becomes rapid and thready and sometimes imperceptible The blood pressure falls to a point where it is difficult to determine and the temperature is usually subnormal but not in every case in burns it may be elevated Respirations tend to become rapid shallower than normal and the external muscles of respiration come into play The output of urine drops to zero The pulse becomes weaker and more thready and finally the patient passes from a semicomatose state into one of complete coma unless something dramatic is done therapeutically the patient surely will die

Such a clinical picture as this may be caused by disorders other than genuine shock but further investigation of the case usually tends to bring out the proper differentiation (1) The veins of the neck are collapsed and empty and the heart smaller than normal rather than dilated in contrast to heart failure (2) in shock the blood volume is decreased while in acute heart failure pneumonia and other conditions causing a similar clinical picture there is no decrease in blood volume (3) the velocity of blood flow is diminished in shock while it may not be diminished in other conditions or not decidedly so (4) hematocrit studies in shock usually show increased concentration while in other clinical entities this occurs much less commonly (5) venous pressure is decreased in shock In acute heart failure and other conditions simulating shock the venous pressure is either normal or increased (6) plasma proteins are definitely reduced in shock while in heart failure and in other conditions they are positively increased or normal (7) the mean corpuscular volume is normal *in shock or slightly diminished while it is* increased in heart failure (8) there is a hyperpotassemia in shock which is absent in other conditions and the sodium of blood is usually decreased or normal in shock In other disorders the blood sodium is normal or higher than normal as a rule (9) recent studies have revealed consistent biochemical changes in patients suffering from shock—medical traumatic and hemorrhagic A definite corre

e *Stimulants as strychnine 2 mg (1/30 grain) repeated every two or three* hours for several doses have been helpful in cases especially those following infections Coramine 5 to 10 cc may be given intravenously

f The use of the vasoconstrictor drugs as epinephrine 1/2 to 1 cc. of a 1 1000 solution pituitrin 1/2 to 1 cc hypodermically or ephedrine sulfate 46 mg (3/4 grain) orally is indicated when shock is due to hemorrhage

2 Special Aids

a As the chief deficiency consists in a low blood volume augmentation of blood volume is a primary requisite in treatment This is achieved by an immediate introduction of fluids intravenously and especially by transfusion of whole blood or in some cases plasma Whole blood *is the ideal method of restoring blood volume but the procedure* involves time and expense and more available measures may be necessary in emergencies *Hypertonic glucose intravenously 50 cc. of 50* per cent solution will hasten the return of fluids into the circulation This injection should be followed by the intravenous administration of two liters of five per cent glucose in physiological saline Normal saline 1000 cc. given intravenously may help to make up the loss of fluids in the vascular system Of course as the capillary wall is more permeable than normal such fluids will not be withheld in the circulation and transfusions are better

b Oxygen is of special importance and should be introduced as soon as possible

c Adrenal cortical extract 20 to 30 cc injected intravenously two or three times a day in the hands of some observers has proved a very effective remedy while others have not observed its beneficial effect. It should be used in every case of shock or threatenings of shock.

d Attempts have been made to improve the venous pressure by applying bandages to the extremities *This type of treatment has been praised by* some condemned by others and considered of very doubtful value by *most investigators*

It may easily be seen that the treatment of shock is quite different from the treatment of conditions simulating it since introduction of fluids in heart failure is contraindicated and only whole blood transfusions are helpful in making up lost blood in hemorrhage One should keep in mind that the shock syndrome is characterized chiefly by a diminished blood volume and this volume must be restored and hemoconcentration which is pronounced must be overcome by more blood dilution

laries and the heart was rapid and appeared weak only because it did not have enough volume of blood to pump effectively

The clinical evidences of shock may simulate the effects of severe hemorrhage While they may have certain features in common the following are points in differential diagnosis the concentration of the blood in hemorrhage is unchanged at first but later becomes lower due to the passage of fluid from tissues into the circulation Nitrogen retention is not present and hyperpotassemia is lacking The differential diagnosis of these three conditions would be quite unnecessary unless the modes of treatment were affected by the diagnosis

Proper treatment varies in important essentials depending upon whether one is dealing with a patient with heart failure shock or hemorrhage

Peripheral Vascular Collapse This condition which is sometimes referred to as peripheral circulatory failure has at times been erroneously called shock While the condition simulates shock there are two distinct factors to differentiate the conditions The blood volume is not reduced in peripheral vascular failure as in shock and the patient with peripheral vascular failure begins to respond favorably within an hour The blood pressure rises the pulse slows down and the pallor lessens Shock on the other hand lacks these responses within an hour and transfusions plasma or both are necessary

TREATMENT

Treatment may be divided into (1) general measures and (2) special therapeutic aids

1 General

a Elevate the foot of the bed

b Apply external heat in the form of hot water bottles and warm blankets or a heated cage It is well to remember that warmth is necessary but may be overdone It has been pointed out that too much warmth is accompanied by vasodilatation and increase in capillary permeability

c Morphine sulfate 16 mg (¼ grain) should be administered hypodermically in cases of pain and restlessness but should not be given when the patient is quiet as there is danger of depressing the respiratory mechanism

d Hot coffee may be administered orally or rectally

3 Deficiency of blood formation
  a Deficiencies due to specific essential factors
    (1) Lack of the antipernicious anemia factor (Macrocytic hyper chromic anemia—lack of extrinsic factor in diet as in the pernicious anemias of pregnancy and sprue as well as deficiency of intrinsic factor as in true addisonian pernicious anemia)
    (2) Lack of iron (Microcytic hypochromic anemia as seen particularly in middle aged women and infants from defective diet and diseases of the gastrointestinal tract)
    (3) Vitamin deficiencies particularly lack of vitamin C as in scurvy
    (4) The deficiency of a specific hormone as thyroxine in myxedema
  b Defective formation due to infections and toxic conditions as
    (1) Bacterial—typhoid fever rheumatic fever endocarditis syphilis sepsis nephritis
    (2) Chemical—arsenic or benzol poisoning x rays radium
    (3) Neoplasms—cancer
  c Disturbances of bone marrow (exhaustion or destruction)
    (1) *Primary aplastic anemia*
    (2) Myelophthisic anemia
    (3) Leukemia and other blood diseases disturbing the erythropoiesis

From the classification above the diseases that may require prompt accurate and effective diagnosis and immediate treatment will be discussed

Acute Blood Loss

When acute hemorrhage occurs the resultant anemia is dependent upon the rate and volume of the blood loss In certain individuals if there is a blood loss of about one fourth of the entire volume collapse and even death may ensue if the loss is gradual a great deal may be lost without causing any severe disturbances It is important to remember therefore that there is a great individual variation in the tolerance exhibited by patients to hemorrhage

Usually the demand made upon the bone marrow by the loss of blood is responded to within 24 to 48 hours after acute hemorrhage and the bone marrow starts regenerating the lost blood cells The speed with which the blood returns to normal depends upon the amount of blood lost whether the hemorrhage is completely stopped and the ability of the bone marrow and other centers of formation to respond to the call for action

Signs and Symptoms When one approaches an individual who has had sudden serious blood loss the clinical picture is quite char

CHAPTER II

Diseases of the Blood

Most of the diseases of the blood do not constitute any condition of emergency Nevertheless most of the blood dyscrasias may be characterized by acute episodes either at the beginning of the disease or at some time during the long slow chronic course In these pages attention will be given to those diseases in which the acute phases are encountered

THE ANEMIAS

Although anemia in its strict sense signifies a lack or want of blood its clinical usage means reduction in the amount of hemoglobin or red blood cells or both Within recent years so much has been achieved in the diagnosis and treatment of the anemias that only the salient features will be considered here Due to the fact that there are so many groupings and terms used in describing the anemias I believe that a classification may be given first in order to expedite the following pages While this outline is not meant to be detailed enough for a hematologist from the practical clinical aspects it has been of aid in gaining a general picture of the anemias

1 Loss of blood
   - *a* Acute—severe hemorrhage as hematemesis wounds hemoptysis and postpartum hemorrhage
   - *b* Chronic—long continued slight bleeding as in peptic ulcer menorrhagia and hemorrhoids
2 Hemolytic anemias or blood destruction
   - *a* The acute hemolytic anemias
      - (1) As in acute febrile conditions such as streptococcal septicemia or endocarditis
      - (2) Toxic in origin as from the sulfonamide drugs
      - (3) *The acute hemolytic anemia of unknown origin*
   - *b* The chronic hemolytic anemias
      - (1) Acquired type which comes on in later life characterized by microcytosis jaundice splenomegaly and increased fragility
      - (2) Familial type commencing during childhood the patient being more jaundiced than ill throughout a lifetime

the contents of two or three nembutal or sodium amytal capsules are dissolved in 15 or 30 cc (½ or 1 ounce) of water and given as a retention enema The patient should be kept in a quiet darkened room and maintained in the twilight zone of consciousness until bleeding is under control

5 Fluids should be given in an attempt to restore the blood volume Of course blood transfusion is the best possible method of achieving this but normal saline or glucose solution or better still 1000 cc of five per cent glucose in saline may be given intravenously at the rate of 10 to 15 cc per minute

6 Blood pressure should be taken every two hours to determine the response of the patient to treatment

7 The pulse rate and heart tone should be carefully examined every two hours

Acute Hemolytic Anemia

This clinical entity is one of the rarer hematological states that might be classified as an acute medical emergency The hemolytic anemias include a rather large number of hematological conditions that represent a more rapid destruction of red blood cells than can be produced by the bone marrow

Etiology There are many etiological factors the commonest of which are severe infections drugs chemicals vegetable and animal poisons hemolysins agglutinins and hemoglobinuria Many cases are familial while others must be considered idiopathic in origin The pathogenesis of this type of anemia in most instances is rather vague and presents a great problem to the hematologist Various theories have been propounded including (1) a marked increase in fragility in red cells and (2) hematoallergic or individual idiosyncrasies which result in the rapid hemolysis of cells Kracke sets forth in his textbook the belief that hemolysis of red cells occurs in two ways (1) By the action of toxic agents on the cells in the peripheral blood and/or (2) by the phagocytic activity of endothelial cells There has been a general shift in emphasis from the bone marrow and a faulty kind of erythropoiesis to the spleen and activity of various hemolytic agents on the mature erythrocyte

Pathology Pathological studies of the parenchymal organs in these cases may reveal a marked deposition of hemosiderin The kid

acteristic In addition to appearing prostrate and agitated the patient s lips and entire body are pale and almost bloodless and may be covered with a slight cold sweat The pulse is thready rapid and weak and the blood pressure falls The condition of the pulse and blood pressure and the rate of breathing constitute the most important criteria in determining the severity of the hemorrhage While the blood count itself and even the determination of the plasma and total blood volumes are important in telling us how much blood has been lost the pulse blood pressure and respirations tell us something even more important—that is how well the patient is tolerating the loss of blood

Although it is important to make a diagnosis of the cause of the hemorrhage especially in the acute type it is more important to take care of the patient first and determine the cause of bleeding afterwards if the cause is not perfectly obvious on superficial examination Bleeding from the bowel is often the result of an acute painless and undiagnosed peptic ulcer Other things as Meckel s diverticulum and bleeding carcinomas may also be painless Tarry stools should always be sought in cases of obscure hemorrhage and careful blood examination should be made as soon as possible to rule out as far as practicable blood disorders that may lead to hemorrhage

TREATMENT

The treatment of hemorrhage may be dealt with briefly It is based upon certain physiological principles

1 An attempt must be made to stop up the hemorrhaging area and to produce a clotting of the blood at the point of hemorrhage How to accomplish this is a problem that must be decided by the kind of case with which one is dealing

2 Sometimes thromboplastin in from 20 to 50 cc doses may be given intravenously to aid the natural processes of coagulation

3 The patient s blood must be typed as soon as possible a suitable donor obtained and provisions made for an immediate transfusion if it is necessary Blood plasma albumin acacia or gelatin may be given in lieu of a blood transfusion

4 If the patient is restless and anxious morphine sulfate 16 mg (¼ grain) must be given at once and the effect continued by the administration of nembutal or sodium amytal by rectum Usually

number (5) *Increased icterus index with an indirect Van den Bergh* and increase in urobilinogen in both stools and urine Hemoglobinuria has been recognized as a complicating feature but is not present in every case When present, it may result in severe kidney damage and thereby produce uremia or even death (6) Presence of spherocytosis in familial hemolytic anemia associated with increased hypotonic fragility (7) A markedly active granulocytic series and an attempt of the erythropoietic series of the bone marrow to regenerate *destroyed cells*

Neber and Dameshek have also reported an aid to diagnosis by the use of bovine albumin solution as a testing and diluting medium for the detection of abnormal isoantibodies in the serum of various cases of hemolytic anemia

Acute Hemolytic Anemia of Lederer Another very interesting type of acute hemolytic anemia is that described by Lederer in 1924 While some hematologists consider this a distinct entity many feel *that this disorder is merely an acute hemolytic anemia of unknown* origin which subsides suddenly Its frequent association with infections suggests this as being the inciting factor The onset is usually that of a rise of fever chills general malaise headache and generalized muscle aches diarrhea and abdominal pain following which a severe anemia and the above described blood picture are noted The important practical feature of this disease is that it usually responds very dramatically to single or multiple transfusions although it is *known to subside without this therapeutic measure*

Acute Febrile Anemia Acute febrile anemia deserves mention when speaking of hemolytic anemia as it is differentiated from the other forms by exclusion It is most frequent in younger people under 20 years of age The onset is abrupt with fever of 101° F to 103° F chills headache vomiting jaundice and sometimes peripheral vascular collapse Hemorrhage from various internal organs may be seen from time to time The most characteristic feature of course is the change in the blood picture The rapid falling off of the red blood cells to one million per cubic millimeter or less may occur within a period of a day or two Nucleated red blood cells are present in the blood smear and the number of reticulocytes increases rapidly Neither the leukocytes nor the platelets however seem to be involved At necropsy the striking features seen are hemosiderosis

neys show a plugging of the renal tubules and may at times even show tubular degeneration This type of kidney pathology corresponds very closely to that seen in the kidneys after transfusion with incompatible blood, which suggests the fact that agglutination of red cells may occur prior to red cell hemolysis

There is an excessive load on the tissues as the result of the destruction of erythrocytes The reticuloendothelial system becomes congested and hyperplastic with the spleen showing marked engorgement of the pulp with red blood cells

Signs and Symptoms An increased output of the bone marrow is resultant after an excessive red blood cell destruction and it is only when there is lack of compensation for excessive destruction that signs of anemia appear Clinically the course of this disease is usually characterized by a sudden rise of fever marked pallor weakness general malaise dyspnea profound anemia and slight icterus usually visible only in the sclerae The spleen which is often tender is usually felt one to three fingerbreadths below the left costal margin The neck vessels pulsate vigorously and there is marked tachycardia Some cases develop rapidly and within a few hours there is extreme weakness dyspnea and semicoma In other instances the weakness and dyspnea appear insidiously Gastrointestinal symptoms are common

The clinical picture as described is the one most commonly seen when the anemia is the result of exposure to chemicals drugs or poison more specifically and more commonly seen recently with the advent of sulfonamide therapy The chief offenders of the latter group are sulfanilamide sulfapyridine and sulfathiazole It is believed that sulfanilamide may produce this complication in two to three per cent of children and eight to nine per cent of adults treated

Diagnosis There are several reliable methods by which a diagnosis of hemolytic anemia may be obtained (1) Rapid decrease in hemoglobin and red count without any evidence of blood loss (2) Leukemoid range of leukocytosis and often the total white count (40 000 to 60 000 white blood cells per cmm) (3) Increased platelet count (4) Changes in the differential blood smear Increased and persistent reticulocytosis at times as high as 60 per cent and increased number of *normoblasts sometimes* exceeding white cells in

Etiology and Pathology Although acute aplastic anemia may be due to such things as benzol arsenic radium and severe infections there is a kind that is quite commonly known as the idiopathic aplastic anemia in which the cause is unknown The red bone marrow is extremely aplastic consists of little more than fat and contains very few cells Some islands of hyperplasia may be found however The spleen is fibrous the malpighian corpuscles are small and the cells of the pulp are few

Signs and Symptoms The clinical features of the disease are centered around the anemia but hemorrhages may arise from the thrombocytopenia and necrotic lesions of the mucous membranes may result from lack of polymorphonuclear leukocytes The chief complaint is progressive weakness preceded by fatigability The patient appears pale but the yellowish tint of pernicious anemia is entirely lacking Weight loss is rare Occasionally the eyegrounds show signs of hemorrhage

Diagnosis This disease must be differentiated from several others that present a somewhat similar picture on the surface For example

1 Agranulocytopenia which is characterized by a pronounced diminution of the polymorphonuclear leukocytes but by fairly normal red blood cell count and normal platelet count The response to treatment is quite satisfactory

2 In certain stages of pernicious anemia the picture may simulate that of the aplastic form However the case history with the characteristic features of pernicious anemia as glossitis achlorhydria neurological changes and the classical blood and bone marrow picture serve to identify it

3 The bone marrow destruction due to certain poisons as x ray and radium must be remembered Acute leukemia must always be given consideration in these blood diseases with features of the aplastic type

Before the era of bone marrow examinations many cases of what is now called hypersplenism were diagnosed as aplastic anemia These were really not cases of aplastic anemia in any sense of the word because the bone marrow is hyperplastic Splenectomy will usually effect a cure in these patients In true aplastic anemia the spleen is usually not enlarged

hyaline thrombosis of the capillaries splenic infarction and hyper plastic bone marrow

Prognosis The prognosis in general for all the acute hemolytic anemias is fairly good if the process is recognized early and treated adequately If not identified and vigorously treated death may ensue

TREATMENT

The treatment is in general very gratifying and consists of the following

1 Adequate alkalinization accomplished by giving sodium bi carbonate 3 to 6 Gm (45 to 90 grains) orally or a 6/M solution of sodium lactate intravenously (usually 600 cc are given) Giving large amounts of fluids rapidly is a dangerous practice

2 Many physicians feel that a great number of transfusions given over many weeks is definitely harmful to the patient and that if a few transfusions given early do not result in recovery or improvement the number should be greatly restricted and given only when the patient *is very anemic*

3 Discontinuation of offending drugs such as any of the sul fonamides

4 Any therapy necessary for the underlying infectious process or for the chemical or poison which may be the etiological agent

5 At times the addition of liver extract 3 to 4 cc intramuscu larly and the administration of ferric ammonium citrate 1 3 Gm (20 grains) three times a day is beneficial although there is no real physiological basis for their administration

6 The results of splenectomy are often dramatic but occa sionally this procedure has no effect on the course of the disease and the hemolytic process continues with a fatal outcome

Acute Aplastic Anemia

Aplastic anemia may be defined as that form of anemia which is characterized by deficient or totally absent blood formation There is a leukopenia of 1500 white blood cells or less at times and anemia *of less than 2 000 000* and the platelet count drops to low figures as 30 000 20 000 or 10 000 per cubic millimeter The course of the disease is frequently rapid and death may occur within a period of a few weeks or months

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Wintrobe states very clearly however that at times a final diagnosis of idiopathic anemia cannot be made until all forms of treatment have proved to be of no avail and the necropsy findings confirm the clinical impression

Prognosis In the idiopathic form of aplastic anemia the course is rapidly fatal and death usually ensues in a few weeks although one may live for as long as 6 months with this condition

TREATMENT

Treatment consists in the following

1 Removal of the cause of anemia if possible

2 Repeated small transfusions

3 Absolute rest and intelligent feeding

4 Slow intravenous or intramuscular injection of pentnucleotide 10 cc (0 7 Gm) diluted to 100 cc with warm sterile saline every day

5 Yellow bone marrow in doses of 20 to 30 drops three times a day

6 Liver extract 2 to 4 cc intramuscularly daily and iron and arsenic in the form of iron cacodylate 32 mg (½ grain to 1 cc) intravenously two times a day

7 Folic acid 10 to 30 mg three times a day

8 Penicillin in suitable dosage to protect the patient from infection

LEUKEMIA AND OTHER DISTURBANCES OF THE WHITE BLOOD CELLS

Leukemia may be defined as a condition characterized by widespread hyperplasia of the leukopoietic tissues throughout the body associated with both qualitative and quantitatives changes in the circulating white cells of the blood Although leukemias have been known since *1845 when Virchow described leukocytic involvement* of the tissues the outlook and treatment have changed little since that time

From the practical point of view leukemia may be divided into the acute and chronic forms the former consisting of three types Lymphatic myelogenous and monocytic The differentiation of these forms is more a manifestation of diagnostic strength than of

practical value as far as the patient is concerned for treatment and prognosis are about the same in any of the acute forms

Acute leukemia is most often found in children or adolescents though many cases have been reported in adults As a general rule acute lymphoid leukemia occurs in children while acute myeloid leukemia and more often chronic leukemia are found in adults In the lymphatic forms there is a decided dominance of male inci dence

Etiology and Pathology The etiology is practically unknown Most investigators agree that it is a manifestation of malignant changes in the blood forming organs Furth in 1935 injected an emulsion made of the spleen of a rat with acute leukemia into other rats In some malignant tumors of the bone marrow formed and in others there were definite evidences of leukemic changes He con cluded that leukemia is a malignancy and not due to inflammatory or infectious disorders We do not know however just what trigger factor starts the sudden proliferation of the blood cells which is seen in acute leukemia There is a hereditary tendency and it has fol lowed trauma pregnancy and malaria

The pathological changes in all forms are very similar the main difference being that in lymphatic leukemia the lymphatic mechanism is very decidedly enlarged while in the myeloid variety this system is not necessarily prominently involved except for splenomegaly

Signs and Symptoms The onset is similar to that of an acute infection with continued high fever chills weakness headache general distress and a rapidly developing pallor There is slight enlargement of the spleen and lymph nodes especially those asso ciated with the mouth throat or respiratory system The lips and gums become thickened and swollen and there are ulcerations in the tonsillar area The skin and mucous membranes bleed easily Hemorrhages are quite common with resulting anemia and retinal changes

The course is usually stormy and characterized by a rapid progres sion of the symptoms It must be remembered that in acute leukemia not only the blood forming organs and blood are involved since microscopic examination shows leukocytic infiltration of the heart muscle kidneys liver and digestive system The urine usually con tains albumin and casts as well as leukocytes and red corpuscles

Pleural effusion and dyspnea often appear and the heart s action may be impaired Jaundice and heart failure frequently complicate the clinical picture of acute leukemia The brain and meninges too may become infiltrated and often the patient will have a stiff neck confusing the picture of leukemia with that of meningococcic meningitis

The blood picture reveals many immature leukocytes and blast cells and there is a rapid rise or fall of the number of circulating leukocytes

Diagnosis Diagnosis of acute leukemia can be made only after numerous disorders have been considered and the various systems of the body carefully analyzed If the typical blood changes are pres ent the diagnosis is easy but frequently we see a case where the white cell count is 8000 rather than 20 000 to 30 000 The differential count may show a normal number of neutrophiles lymphocytes and monocytes and sometimes a careful search fails to uncover a blast cell This condition is called aleukemic leukemia The changes in the bone marrow and lymph glands are present but the blood does not reflect these abnormalities Repeated examinations however usually uncover blast cells of some type

A clear cut case of acute leukemia includes a pale skin hemor rhages skin lesions characteristic blood changes of an extremely high white blood count with many blast cells marked anemia and low platelet count and enlargement of both the spleen and lymph nodes (particularly in the lymphatic form)

Differential Diagnosis In differential diagnosis such diseases as infectious mononucleosis Vincent s angina typhoid pneumonia endocarditis acute rheumatic fever diphtheria meningitis and a number of other acute infectious disorders must be considered Perhaps the most confusing condition is acute infectious mononucle osis in which the white cells are greatly increased (20 000 to 40 000) Eighty per cent as a rule are lymphocytes of a youthful variety and the differentiation between these and stem cells is occasionally diffi cult to make Sore throat swollen lymph glands an enlarged spleen jaundice fever and many of the features of acute leukemia are pres ent However the lowering of the platelet count does not occur and there is no anemia or prostration The course is benign and not stormy

In infectious mononucleosis the diagnosis is verified by the finding of a positive *heterophile* antibody reaction The *patient with* infectious mononucleosis usually recovers and the one with acute leukemia does not and therefore the differential diagnosis is of great importance in outlining the course and prognosis

Prognosis Prognosis in all types of acute leukemia is gloomy The course is usually rapid and characterized by weakness hemorrhage prostration fever collapse stupor and coma Death occurs in from three weeks to two months If the patient lives longer than that the disease is likely to be an acute exacerbation of a chronic leukemia rather than the acute form As a rule the older the patient the better the chances are for longer life If there are no other complications and if the leukocyte count is low the prognosis is comparatively good In some cases the symptoms disappear and the patient seems to be quite well and then in a short time the symptoms reappear and there are frequent remissions until the patient dies

TREATMENT

X ray treatment of the long bones and spleen is used but it is the opinion of many physicians that it may be definitely harmful and hasten the patient s death Radioactive isotopes of phosphorus and *sodium have been used without any more beneficial effect than x ray* Urethane nitrogen mustard aminopterin and tyrosinase have also been used without producing substantial change in the clinical course

The clinical management of acute leukemia has been greatly helped with the introduction of penicillin and drugs which will control the *hemorrhagic manifestations Penicillin in satisfactory doses* should always be given for the control of infection to forestall the development of offensive and painful necrotic lesions so characteristic of the disease Rutin in doses up to 80 mg three times a day will sometimes greatly reduce the hemorrhagic tendency as will protamine 2 5 mg per kilogram of body weight given intravenously daily

Transfusions should be given to keep the patient as comfortable as possible but these should be eliminated if symptoms of severe anemia develop

Acute Monocytic Leukemia

In 1913 Schilling and Reschad gave an account of monocytic leukemia that form which is characterized by widespread hyperplasia

of the tissue from which monocytes are derived by increased cells in the blood stream and by their deposition in various tissues and organs Although many authors have called this type of leukemia the third form of leukemia in association with the chronic myelog enous and chronic lymphatic kind described by Virchow and the acute myeloblastic leukemia of Naegeli there are some who be lieve that monocytic leukemia is merely a phase of myelogenous leukemia

Etiology and Pathology Monocytic leukemia is the center of high controversy because the origin of the monocyte is obscure At present it is admitted that most probably the monocyte may be derived from several sources in which case there is the possiblity of several types of monocytic leukemia Two types are recognized (1) Naegeli type and (2) Schilling type

The Naegeli type is centered in the myeloblast In this case the monocytic leukemia is a variant of myelogenous leukemia The monocytic phase usually reverts to the picture of myelogenous leu kemia before the course of the disease is run

The Schilling type is centered in the reticulum cell There is a hyperplasia of the reticulum cells These cells round off and become free In the case of monocytic leukemia these free cells develop into the monocyte that is found in the peripheral blood stream It is conceded that this is the same as the leukemic reticuloendotheliosis of Ewald developing toward the monocytic line

The Naegeli type and the Schilling type of monocytic leukemia can be differentiated by a careful study of the cells intermediate between the stem cell and the mature monocytes It is usually the Schilling type of leukemia that is referred to as the acute mono cytic leukemia

Signs and Symptoms The clinical course of monocytic leukemia *is relatively acute The presenting symptoms* and the physical find ings are similar to those of other acute leukemic states except that there is a predominance of oral and throat disorders Symptoms re ferable to the teeth are particularly prevalent

Examination reveals a markedly pallorous patient who is acutely ill Also evidenced may be extensive purpura bleeding from the gums which are usually quite hypertrophied and boggy in appear ance diarrhea and enlargement of the spleen

Monocytic leukemia manifests a profound rapidly progressive anemia It is the normocytic normochromic kind with evidences of normal or pathological regeneration

Diagnosis Diagnosis is based on the clinical findings Those cases having a high leukocyte count are easily recognized but this may be extremely variable ranging from 600 to 240 000 cells per cmm The platelet count is low with accompanying manifestations of bleeding

Examination of the bone marrow will clinch the diagnosis because even though the abnormal cells are difficult to find in the peripheral blood if a real leukemic process is present the bone marrow will contain great numbers of blast cells

The blood film reveals varying percentages of monocytes in all stages of development Care must be exercised not to confuse atypical myeloblasts and even atypical promyelocytes with monocytes In the Schilling type of leukemia the monocyte can be traced through intermediate stages to the reticulum It is the intermediate cells that retain the reticular structure in the nucleus

The course of the Schilling type of monocytic leukemia is rapidly progressive and usually of short duration

TREATMENT

Monocytic leukemia does not respond to treatment Deep x ray therapy may alleviate the pressure symptoms of a leukemic mediastinal tumor but such treatment will not aid any of the other symptoms and may even lead to increased neutropenia and anemia Blood transfusions are only palliative and sometimes harmful

Acute Aleukemic Leukemia

Aleukemic leukemia is the source of much confusion and as such has many synonyms such as aleukemic myelosis hypocytic leukemia leukopenic leukemia pseudoleukemia aleukemic lymphadenosis subleukemic leukemia and undoubtedly a few more names It has been defined on the one hand as a disease with a clinical course and organic changes identical with the leukemic state but in which the peripheral blood shows no leukocytosis nor any immature cells at any time On the other hand aleukemic leukemia is considered merely as a leukopenic phase in the leukemic process The adherents of the

latter opinion feel that an accurate knowledge of the morphological appearance of immature cells particularly the blast forms or the stem cells, and a persistent search will reveal varying percentages of these cells at some time or other in the leukemic state which is characterized by a leukopenia

Etiology and Pathology The etiology of aleukemic leukemia like that of other types of leukemia is unknown

Aleukemic leukemia may be chronic subacute or acute in its clinical course It is usually myelogenous or lymphatic in type the latter occurring the most frequently

Aleukemic leukemia is characterized by a profound rapidly progressive anemia The anemia is usually the simple regenerative type showing the presence of anisocytosis polychromasia normoblasts and single Jolly bodies in the red blood corpuscles It is often toxic with the added features of poikilocytosis basophilic stippling and multiple Jolly bodies in the erythrocytes In rare instances the erythrocytes are macrocytic and hyperchromic With the concomitant leukopenia these cases are often confused with pernicious anemia The red blood corpuscles are normal in mean volume and hemoglobin except in cases complicated by chronic bleeding

Signs and Symptoms The chief symptoms are those of a grave anemia namely weakness pallor fatigue dyspnea and palpitation The physical findings are identical with those of other forms of leukemia Necrotic lesions of the mouth are a common feature

Diagnosis In diagnosing a case of acute aleukemic leukemia one may find the total number of leukocytes in the normal range though generally the leukocyte count falls in the leukopenic range Values as low as 400 cells per cmm are not infrequent

A scrupulous morphologic study of the blood smear is imperative In a case of aleukemic leukemia a diligent daily search will reveal at least a few of the stem cells either myeloblasts or lymphoblasts and the presence of myelocytes and promyelocytes if the case is myelogenous in type

The platelet count is usually reduced below the critical level with the accompanying findings of hemorrhage and petechiae The platelets however may be within the normal range

Differential Diagnosis Aleukemic leukemia may be confused with other diseases characterized by a leukopenia among which are agranulocytic angina severe sepsis idiopathic aplastic anemia Banti s

disease, pernicious anemia thrombocytopenic purpura metastatic carcinoma and Hodgkin s disease A bone marrow biopsy with a careful morphological study of the bone marrow cells and a scrupulous examination of the peripheral blood will establish the correct diagnosis in the great majority of these cases

Agranulocytic angina seldom if ever has an anemia or a thrombocytopenia comparable with that usually found in aleukemic leukemia Likewise myeloblasts and promyelocytes or lymphoblasts and early lymphocytes are not encountered in the blood films of agranulocytic angina to any significant degree The majority of cases of agranulocytosis in the hyperplastic phase with a maturation arrest at the myeloblast stage may cause difficulty in arriving at the correct diagnosis from the bone marrow study alone The continued study of the peripheral blood will solve the problem

Severe sepsis can be differentiated from aleukemic leukemia by the absence or only the rare appearance of the blast forms and promyelocytes in the peripheral blood stream There is a shift to the myelocyte and the promyelocyte stage of the granular series in the bone marrow in sepsis but seldom does the bone marrow show a great predominance of myeloblasts promyelocytes or lymphoblasts as is characteristically encountered in aleukemic leukemia

Idiopathic aplastic anemia discloses an aplasia of the bone marrow or at least a marrow with a predominance of the leukemic cells Aplastic anemia reveals no signs of regeneration in the blood stream In aleukemic leukemia signs of normal and pathologic regeneration are usually present

Banti s disease pernicious anemia thrombocytopenic purpura metastatic carcinoma myelofibrosis and Hodgkin s disease rarely manifest blood cells younger than myelocytes in the peripheral blood If myelocytes occur in these conditions they rarely exceed 15 per cent of the total leukocytes

The characteristic appearance of the erythrocytes usually called megalocytes the distinctive changes in the appearance of the neutrophiles and the hyperactive megaloblastic bone marrow of pernicious anemia will distinguish pernicious anemia from aleukemic leukemia in almost every case

Thrombocytopenic purpura shows an increase of the megakaryoblasts and megakaryocytes in the bone marrow and a normal or slight hyperactivity of the granular series and the normoblastic series which

is in no way comparable to the picture found in the leukemic state

Metastatic carcinoma also may reveal a hyperactive bone marrow but here again the marrow rarely shows a predominance of the stem cells (myeloblasts or lymphoblasts) and the early promyelocytes

Hodgkin s disease will be differentiated from aleukemic leukemia by the characteristic tissue changes found in this disease as revealed by histological study In addition histoplasmosis and leishmaniasis should be considered in the differential diagnosis

The course of aleukemic leukemia is the same as that in other leukemic states

TREATMENT

Acute leukemia is resistant to all treatment The pressure symptoms of a leukemic mediastinal tumor may be relieved by deep x ray therapy This treatment however, will not alleviate any of the other symptoms and even small doses may quickly add to the neutropenia and anemia Blood transfusions are worthless and may occasionally make the condition worse

INFECTIOUS MONONUCLEOSIS

Infectious mononucleosis or glandular fever as it is sometimes *called* is an acute and often contagious disease *characterized by glandular enlargement and fever though these need not be present*

Etiology Although the *Listerella monocytogenes* has been isolated from the peripheral blood or cerebrospinal fluid in many cases the cause of infectious mononucleosis is unknown This syndrome most often occurring in childhood can be acquired by contact and although proof is lacking some authors believe it to be related to influenza leukemia or streptococcus infections It is the opinion of most investigators at the present time that infectious mononucleosis is caused by a virus which as yet has not been isolated

Pathology Examination of lymph nodes reveals a variation in size and shape of the lymphocytes They have a characteristic pattern which distinguishes them from other lymphocytes Usually there are general hyperplasia and dense foci of rounded reticulum cells which fill the sinuses In advanced stages follicles and germ centers are often absent There are characteristic changes in the leukocytes In about 50 per cent of cases the spleen is enlarged and the necrotic

lesions found in the liver simulate those of infectious hepatitis suggesting the possibility of a virus infection

Signs and Symptoms Fever enlargement of the lymphatic glands sore throat changes in the blood cells and enlargement of the spleen usually form the clinical picture of infectious mononucleosis A small percentage of cases develop jaundice which is attributed to the hepatitis that develops Since it resembles so many other diseases it is rather difficult to list the symptoms The onset varies The patient may be conscious of a vague constitutional illness for several days but because it is so mild a physician is not consulted Then fever and general malaise set in followed by other symptoms and finally glandular enlargement Usually the onset is sudden with chill and rapid rise of temperature and the disease runs an acute course for two to four weeks and then subsides Headache dizziness or faintness irritability purpuric eruptions and skin rash fatigue anorexia sore throat malaise and general weakness are commonly present Pain in the joints and throughout the body particularly in the neck abdomen and gastrointestinal tract are occasional symptoms The leukocyte count may vary from a leukopenia to a leukocytosis of 30 000 hemoglobin and red blood count are usually within normal limits

Fever continues for a week or more commonly rising in the afternoon The temperature varies from 37 2 to 40 C (99 to 104° F) the pulse rate runs parallel with the temperature as 92 beats per minute with a fever of 39 C (102 F) The enlargement of the glands may start before during or weeks after the fever sets in and it may continue for a few days or several months The enlargement varies in size from 1 to 2 cm in diameter to that of a small plum The cervical and inguinal glands are involved most often though cases have been reported of enlargement of the axillary and mediastinal glands

There is some question as to whether an attack of infectious mononucleosis may have an effect on the heart it is generally conceded that acute cardiac failure may result if the heart is in poor condition previous to the attack

Diagnosis Pyrexia splenomegaly adenopathy and mononuclear leukocytosis indicate the diagnosis When the classical picture of glandular enlargement and fever is present the blood should be

examined If there is a great increase in the mononuclear cells with abnormal lymphocytes varying in size structure and staining properties infectious mononucleosis may be suspected The Paul Bunnell test will clinch the diagnosis This test should always be done in patients with false positive Wassermann reactions or with positive agglutination tests without cultural proof

The differential diagnosis formerly constituted one of the difficult features of the disease The swollen lymph glands enlarged spleen and increased white count with preponderance of lymphocytes often led to a diagnosis of acute lymphatic leukemia Hodgkin s disease granulocytopenia typhoid fever and tuberculosis have all been confused with infectious mononucleosis Since the work of Longcope and Downey in 1923 the blood picture has been more widely recognized and the differential diagnosis made easier In addition to this the laboratory aid of Paul and Bunnell described in 1932 is practically diagnostic because the presence of heterophile antibodies in the blood can be noted

Prognosis in uncomplicated infectious mononucleosis is very good and for this reason correct diagnosis is important

TREATMENT

1 The treatment is symptomatic and consists primarily in forestalling complications as bronchitis pneumonia or any upper respiratory tract infection

2 Sulfadiazine has given quick and permanent relief in some cases The initial dose is usually 4 Gm (60 grains) followed by 1 Gm (15 grains) every four hours until the optimal level is reached in the blood stream and then 1 Gm (15 grains) three or four times a day *may be given until the fever subsides This treatment is especially* good when there are complications as hemolytic tonsillitis or respiratory infections

3 Convalescent serum may help but it is not usually available

4 Sodium perborate as a mouth gargle used prophylactically is indicated because Vincent s infection is often present in conjunction with infectious mononucleosis If the spirilla and bacilli of Vincent are found neoarsphenamine (five per cent in glycerin) may be applied locally

5 Penicillin 25 000 units every three hours is now widely used

because it cleans up the secondary infections in the mouth and throat quite rapidly

HEMOPHILIA

Hemophilia is a hereditary blood disease occurring only in males but transmitted by females in whom the tendency to bleed exists as a mendelian sex linked recessive defect It is characterized by prolonged coagulation time and repeated hemorrhages throughout life It has been suggested that since men are subject to the disease and women are not the latter must have some substance in their bodies which is absent in males This may be an ovarian or estrogenic element or a substance in the placenta that may hasten the coagulation time because young infants bleed rarely or not at all and still grow up to be hemophiliacs

Etiology According to mendelian principles a woman may be a true hemophiliac if she is the daughter of a hemophilic male and a hemophilia transmitting woman However such a union is rare and it is probable that such an inheritance factor would be fatal to the fetus The transmission of the disease is dependent on the parents The marriage of a normal man and a female carrier results in half the sons being bleeders and half the daughters being carriers There is no way of telling which daughters are carriers until they have children The transmission of the disease by the union of a hemophilic male and a healthy female results in all daughters being carriers so all male grandchildren of the original union may be bleeders but the male offspring of the original union will not be bleeders

It has been noted that the hemophilic families are usually above the average in size Most hemophiliacs have more daughters than sons a ratio of about 2 to 1 and those daughters who are carriers have more sons than daughters thus accounting for the perpetuation of the disease It rarely occurs in Latins but it is common in the English and Teutonic races However cases are found the world over especially in young people

Defect in coagulation apparently lies in the blood platelets All of the constituents of the blood are normal in appearance quantity and chemical content It is assumed that the platelets are highly resistant to breakdown and for this reason there is a lack of thromboplastin and coagulation is delayed

Pathology The fundamental lesion in hemophilia appears to be a decreased fragility in the platelets Normally platelets from normal blood that are placed into a paraffined tube disappear within a short period but they may be found intact in hemophilic blood several hours later

Signs and Symptoms The disease is not noted at birth but symptoms usually appear when the child is about two years of age Repeated and severe hemorrhages which are either spontaneous or the result of slight trauma are noted The bleeding is characterized by its persistence and is usually more severe during puberty than after The circumstances of the bleeding vary, the period of bleeding may be slight and short or severe and prolonged and it may continue for a long time or it may be absent for several months The how when where and why of these hemorrhages are questions that are unanswerable at present

Spontaneous hemorrhages may occur in the joint cavities as well as in the muscles and connective tissue The bleeding into the joints knee ankle elbow and hip in that order of frequency is often necessary to clinch the diagnosis Joint bleeding is characterized by diffuse redness marked swelling sudden pain and a varicolored skin over the affected part The pain may become very severe Temporary invalidism, transitory or even permanent crippling restricted movement and slight or marked bone destruction and deformity may result from these attacks Anemia arises as a result of the blood loss the degree being dependent on the duration and severity of the hemorrhages Otherwise there are no signs of the disease and during the periods of remission the patient may appear normal

Diagnosis Diagnosis is comparatively easy since a family history is usually obtainable and the disease occurs in the male sex The bleeding time is normal the coagulation time is prolonged during attacks but is usually almost normal between them The prothrombin time is normal and fibrinogen is abundant The capillary resistance test is normal

Prognosis Because of the severity of bleeding in childhood and of the greater chance of trauma in that period as from (1) falls (2) scratches (3) tooth extraction or loss of teeth and (4) tonsillectomy and the inability to control hemorrhages after they start the prognosis is poor Most patients die before they reach the age of

puberty, but if they live beyond this stage their chances of long life increase Since the patient lives in constant fear of attacks and consequent fatal hemorrhage the mental outlook is poor though he is usually quite well between periods of bleeding Permanent damage to the joints is common Sometimes one attack follows another and the victim remains in a state of invalidism since he is never really able to recover from one siege before another sets in

TREATMENT

There is no specific therapy for hemophilia Treatment is directed more at the prevention of hemorrhage than stopping it after it once begins

1 The individual should be protected from trauma

2 When hemorrhage starts the patient should have absolute rest and quiet small doses of opiates as morphine 8 to 10 mg (1/8 to 1/6 grain) or pantopon 8 to 10 mg (1/8 to 1/6 grain) hypodermically should be given

3 Topical thrombin should be applied locally to the wound to bring about prompt clotting

4 Tissue extracts containing thromboplastin may also be used

5 Adrenalin 1 1000 solution applied locally may be used

6 Compression is indicated in external wounds

7 Fresh cotton wool soaked in fresh normal blood or blood serum should be applied to the wound Fibrin foam and gel foam packs may also be used

8 Blood transfusions usually stop the hemorrhage but the effect is transitory In spite of this blood transfusions seem to be the best form of specific treatment available Consequently multiple transfusions 25 to 100 cc daily or every other day are advisable It is probable that they supply thromboplastin which seems to be lacking in the abnormal blood of the hemophiliac and thus the prothrombin is converted to thrombin more quickly The coagulation time is normal for about five days after transfusion and for this reason transfusions should be given before operation

9 Treatment with estrogenic hormones has been tried with doubtful success

10 The human globulin fraction isolated by Cohn when given intravenously is very effective in controlling the bleeding

CHAPTER III

Diseases of the Blood

(Continued)

AGRANULOCYTOSIS

Agranulocytosis or malignant neutropenia as it is sometimes called is a syndrome which refers to a great decrease or complete absence of the granular leukocytes Though there is no complete unanimity of opinion regarding the most appropriate name for this disease the term agranulocytosis is used here because it is the original one employed and the one most generally understood Other names as (1) agranulocytopenia (2) agranulocytic angina (3) acute primary granulocytopenia (4) mucositis necroticans agranulocytica and (5) agranulosis sepsis with granulocytopenia have been substituted for agranulocytosis

Etiology Age and sex seem to play little part in the etiology of agranulocytosis though it is more prevalent among the well to-do the medical profession and middle aged women Among the middle aged the condition is two or three times as common in women as in men It rarely occurs in Negroes this has been explained by the fact that they seldom use drugs depending more on liniment or some kind of self sacrifice to relieve themselves of pain

Agranulocytosis may be divided into the primary and secondary types The cause of primary agranulocytosis is unknown though it seems to begin as a primary affection of the bone marrow with a marked diminution of granulocytes in the peripheral blood occurring a few days later The causes of secondary agranulocytosis are many Benzene and drugs with the benzene nucleus are known to produce leukopenia *Amidopyrine is closely related to benzene* Madison and Squier observed that in cases of granulocytopenia there was a history of consumption of amidopyrine Other causes which have been listed are endocrine imbalance allergy infections vitamin deficiency susceptibility to certain drugs excessive radiation use of organic arsenical compounds sulfonamide drugs dinitrophenol and the pyrazalon drug group Cortical adrenal defi

ciency and hormonal disorders have been known to accompany agranulocytosis

The fact that this disease has become more widespread recently has been explained by the greater number of drugs on the market and the increased use of them More people are taking drugs containing the benzene ring for the relief of pain and many have substituted these drugs for the salicylates It should be emphasized that it is not the only element which may cause agranulocytosis and that an overdose of amidopyrine does not produce the same symptoms as those seen in agranulocytosis The conclusion may be drawn that an idiosyncrasy to the drug determines whether the person will show signs of the disease Since amidopyrine is known to be a dangerous drug its use should be omitted or at least restricted to cases of severe pain in which other remedies are ineffective The action of the drug is so variable that it is almost impossible to determine the amount which will affect a sensitive person and how much is necessary to cause agranulocytosis

The extraordinary consumption of the sulfonamide compounds has caused many investigators to study carefully their toxic effects upon the blood and bone marrow Leukopenia anemia thrombocytopenia and agranulocytosis have been reported as occurring after the consumption of one of the sulfonamide drugs There is no doubt that the sulfonamides have a pernicious influence on the blood and blood forming organs at times but their great advantages in the treatment of infections so far outweighs the disadvantages that these toxic side effects do not usually warrant permanent discontinuance of the drug Reactions from the use of thiouracil have been observed in which the total white count remains within normal limits but there is complete disappearance of the neutrophilic cell series from the peripheral blood stream However the use of these powerful chemical compounds must always be accompanied by careful and frequent blood studies These tests will assist the physician in keeping the sulfonamide content of the blood at the proper level

Pathology The most striking feature of agranulocytosis is the almost entire absence of polymorphonuclear leukocytes Because of this absence of the cells which normally fight infection necrotic lesions develop in the pharynx mouth and occasionally in the vagina

and rectum The bone marrow usually shows an absence of formation of the polymorphonuclear cells occasionally it may be hyperplastic giving the appearance of a maturation arrest of cellular development The cells which are seen in the bone marrow usually show severe changes of degeneration

Signs and Symptoms The onset of agranulocytosis is usually sudden with high fever chills rapid pulse severe headache general aching and occasionally sore throat and spongy tender gums A sore throat that fails to clear up within a few days should prompt one to study the blood carefully However a rather long prodromal period with increasing malaise lassitude and easy fatigability usually precedes the illness The patients are pale tired and show lack *of interest in their surroundings If treatment is not started at the* onset of the disease diarrhea and ulcerations or necrosis of the throat and other mucous surfaces which are coated with yellowish membrane and accompanied by a foul odor are likely to develop Nausea vomiting epigastric pain and occasionally a rash may occur There is tenderness on pressure over the long bones and sternum

The blood picture tells the entire story of the disease Severe and progressive leukopenia is the main factor and as the result of a shortage of leukocytes and consequent lowered physical condition the patient is subject to infection Sometimes there is a total absence of neutrophiles in the peripheral blood Immature white cells are rare and the total white count is seldom above 2500 per cmm because of the low number of polymorphonuclear cells The bone marrow may either be depressed or show evidence of maturation arrest Anemia and thrombocytopenia are rarely present

Diagnosis The clinical picture of this disease resembles that of the leukemias aplastic anemia infectious mononucleosis diphtheria and septic sore throat However the leukocyte count in agranulocytosis is usually under 2000 cmm with few or no neutrophiles which distinguishes it from the diseases mentioned above Examination of the sternal marrow also aids in diagnosis Acute leukemia may be differentiated from agranulocytosis by the predominating immature white cells and frequent hemorrhages especially in the late stage aplastic anemia is characterized by the

diminution of platelets and progressive anemia Serologic tests should be done routinely for syphilis brucellosis tularemia and infectious mononucleosis

Prognosis The prognosis of agranulocytosis is always serious The disease runs a course of from three to ten days and carries a high mortality unless prompt and vigorous treatment is instituted However the chance for recovery today is much better than it was ten years ago because the condition is usually diagnosed earlier and the treatment is more effective Early diagnosis is important because *if the disease is discovered and treated early and there are no other* infections the patient has a 50 50 chance for recovery It has been noted however that if recovery occurs relapses which are as dangerous as the original attack may take place

TREATMENT

1 All therapy considered to have any bearing on the etiology of the disease should be discontinued

2 In the acute phase of the disease the patient should be put at complete bed rest and given a diet with a high caloric and vitamin content Scrupulous care should be given to the mouth and local lesions and neoarsphenamine or a saturated solution of potassium chlorate may be applied locally to clear up the inflammation of the mouth and fauces Ulcerated areas may also be swabbed with a solution of copper sulfate 0 65 Gm to 30 cc All abscesses should be drained

3 Pentnucleotide solution 40 to 50 cc daily in divided doses should be given intramuscularly Frequently the injections are very painful and cause quite a rise in temperature Occasionally there are also abdominal pain and respiratory distress Pentnucleotide is not a specific drug and many question its therapeutic value However it usually brings about a rise in the white count and in the percentage of polymorphonuclear neutrophiles The amount of the drug may be decreased and finally eliminated after the white count has been normal for several days If there is no response within ten days after initiation of the treatment it is probable that further use of the drug will be of no avail In severe cases 10 cc of pentnucleotide diluted to 100 cc with warm sterile saline solu

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both The name refers to the extravasation of blood into the sub cutaneous tissues which produces petechial hemorrhages or ecchymoses Both are the result of the same fundamental defect The variation in appearance of the lesions is merely a matter of a difference in the degree of severity of the disease

There are so many factors involved in the pathogenesis of purpura so many diseases which have purpura as a secondary phenomenon and so much that is not known about purpura that it is no wonder a physician is confused when confronted with this symptom complex Many classifications of the purpuras have been submitted but few are simple enough and at the same time clear enough to be practical The following classification however has been found workable For our purposes purpura may be divided into the primary (idiopathic) and secondary (symptomatic) types The term primary or idiopathic refers to those cases in which there is no associated disease that may be the cause of the purpura The term secondary is reserved for those purpuras in which there is another disease that is considered the cause of the purpura It is important to keep in mind that the differentiation is not always easy but it is important because the treatment of the two conditions is very different

Primary Purpura

According to Elliott only 42 of approximately 700 cases of purpura were classed as primary or idiopathic Primary purpura may be called essential thrombocytopenic purpura because it is a condition characterized by petechiae or ecchymoses in the skin reduction in platelets and changes in the cells of the capillary wall The hemorrhages occur as a result of these factors and because of the extensiveness of the hemorrhages into the skin and mucous membanes of the lungs mouth and rectum the term purpura hemorrhagica was given the condition by Werlhof (1735) Sometimes certain other diseases produce a thrombocytopenia and purpura which may simulate the essential primary or idiopathic purpura Therefore when thrombocytopenic purpura occurs in an individual a careful search must be made for some other disease that may cause the fall of platelets as leukemia metastatic carcinoma and aplastic anemia Yet these diseases are usually recognized by their attributes other than the thrombocytopenia

tion may be injected intravenously over a period of 20 minutes Following this injection dyspnea palpitation and even chills and fever may develop

4 Desiccated yellow bone marrow 25 drops three times daily has been recommended

5 Transfusions are used by some physicians At any rate this form of treatment is a good supportive measure and it may keep the patient alive until a specific therapy is put to use

6 *Liver extract may be given intramuscularly 4 to 8 cc a day* but its value as a therapeutic measure is *debatable* However, it does no harm and it is believed by some to produce increased delivery of granulocytes in 24 to 48 hours

7 *Stimulating doses of x rays may be used* but the amount of benefit derived is questionable

8 *Sulfonamides should be used in combating the sepsis of agranulocytosis* Going on the premise that patients with agranulocytosis die of the resulting secondary sepsis rather than the reduction of agranulocytes full doses of sulfathiazole given to patients with severe aminopyrine agranulocytosis after the bone marrow has a chance to recover often produce dramatic results Since the sulfonamides act by bacteriostasis they may be given with impunity in conditions with marked leukopenia It is interesting to note that when a sulfonamide drug causes agranulocytosis administration of the drug must be stopped immediately but in all other cases these drugs are valuable therapeutic agents

9 Experiences with penicillin indicate that this drug is the most potent remedy available for the treatment of agranulocytosis and for the prevention or control of the possible fatal complications of the disease Intramuscular administration of 50 000 to 100 000 units of penicillin every four hours results in a cure in from four to ten days depending upon the severity of the case

10 BAL 1 5 cc (10 per cent solution) doses every 6 hours for 18 hours and then 2 cc daily for six doses has been used in treating agranulocytosis following intensive arsenotherapy and gold therapy

PURPURA

Purpura is not a disease *sui generis* but a condition in which there is an alteration of the blood capillaries of the blood or of

formed by placing a tourniquet or cuff of a blood pressure instrument above the elbow and pumping the pressure up above the diastolic level so as to obstruct the venous return but not the arterial flow for about five minutes In purpura where capillary resistance is decreased petechial hemorrhages occur over the entire forearm

5 The white blood cells are normal A pronounced leukopenia or other abnormalities in the white cells would lead one to think of a secondary rather than a primary purpura

The course of the disease may be short for a period of a few months or for a lifetime The disease may be self limited or it may disappear for a while and return at some later date

Prognosis This depends upon the adequacy of the treatment As will be pointed out most of the patients that is 85 to 90 per cent with thrombocytopenic purpura recover It must be borne in mind however that occasionally a patient with a severe grade of the disease may hemorrhage to death die of a cerebral hemorrhage or thrombosis or be the subject of an intercurrent infection

TREATMENT

1 General measures of treatment such as rest in bed good nursing and a well balanced diet are of great value in therapy

2 Splenectomy has been found to be of value in most cases at times it is even a life saving measure If a patient is having severe purpuric bleeding very frequently splenectomy will result in the immediate cessation of the hemorrhage Once the diagnosis is established splenectomy should never be delayed in severe cases

3 Blood transfusions of course are used as a supportive measure and very definitely help to combat shock

4 Focal infections as apical abscesses or sinus infections are contributory factors and should be cleared up but a warning must be sounded in regard *to these procedures attempts at removal of* these foci may cause disastrous bleeding unless the patient is properly safeguarded by either a previous splenectomy or multiple transfusions

5 Many patients with purpura have been demonstrated to have an allergic sensitivity and the removal of the offending allergen from the diet and environment will result in a cure

Etiology The cause of idiopathic (primary) essential thrombo cytopenic purpura is unknown as the name implies though the condition occurs most frequently in children and young adults The important point to be remembered is that other diseases as infections metabolic disturbances and poisonings from drugs must be elimi nated as causes of the clinical picture

Pathology The pathological changes that occur in the spleen and bone marrow are not specific enough to be agreed upon by all authorities The chief abnormal changes have been found in the spleen where the germinal centers are enlarged and active The megakaryocytes of the bone marrow are usually increased in number These cells usually appear to be forming large platelets and also seem to be in a state of maturation arrest

Signs and Symptoms The disease may be acute or chronic The acute condition is much rarer than the chronic and is usually found in young individuals especially females under the age of 40 years The chronic form may occur too but it is commoner in adults and is usually recurrent and milder and may continue intermittently with periods of years between the episodes

The disease usually comes on abruptly with the attention of the patient focused upon bruise marks or small or large subcutaneous hemorrhages In the more severe forms bleeding may arise from the gums or other parts of the body or a menstrual period may fail to terminate as usual and instead continue for several weeks Fever is unusual while rapid heart rate is common The spleen is com monly enlarged but in the early stages it may not be palpable The presence of an excessively large spleen with purpura tends to make one believe that the disease is not idiopathic purpura but leukemia with purpuric manifestations

Diagnosis The exact diagnosis depends almost entirely upon a study of the blood picture

1 The chief feature is a reduction of the platelets from 250 000 or above to 20 000 per cmm or below

2 The bleeding time is increased from a normal of three min utes to ten minutes or more

3 The coagulation time of the blood is normal but the clot fails to retract and there is no extrusion of serum

4 The capillary resistance test is positive This test is per

formed by placing a tourniquet or cuff of a blood pressure instrument above the elbow and pumping the pressure up above the diastolic level so as to obstruct the venous return but not the arterial flow for about five minutes In purpura where capillary resistance is decreased petechial hemorrhages occur over the entire forearm

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5 Many patients with purpura have been demonstrated to have an allergic sensitivity and the removal of the offending allergen from the diet and environment will result in a cure

6 Rutin 10 to 20 mg three times a day or hesperidin 50 to 100 mg one to four times daily will control the purpura of certain individuals

7 Protamine 2 5 mg per kilogram of body weight has been found to be very helpful in some cases

8 X ray irradiation of the spleen will frequently control the disease

Secondary Purpura

In contrast to the purpura of primary essential thrombocytopenia where there is no recognizable cause secondary purpura embraces those purpuras which are due to some underlying disease Most purpuras belong to the secondary group Thrombocytopenia may or may not be present if it is marked difficulty may be encountered in differentiating the secondary type from the primary The important point however is to exert every effort to determine the cause if possible and direct the management of the case at the underlying disease rather than at the thrombocytopenia and purpura directly

Etiology and Pathology Secondary purpura may be divided into two large classes (1) Secondary thrombocytopenic purpura which is caused by some recognized disease that is associated with lowering of the blood platelets Among such diseases are myelophthisic anemia pernicious anemia leukemias aplastic anemia intoxication from x rays radium or drugs (2) The secondary purpura without thrombocytopenia forms the second group In this class if the platelets are reduced at all it is very little and the purpura is predominantly caused by changes in the capillary wall not dependent upon the number of platelets in the blood stream

1 Secondary purpuras may develop as a sequel to infections as cerebrospinal meningitis measles etc

2 Toxic purpuras may be caused by drugs as quinine the barbiturates mercury and the sulfonamides

3 Constitutional debility as seen in chronic glomerulonephritis cancer and syphilis may cause purpura Scurvy and at times other avitaminosis may lead to purpura

4 Well known is the purpura of subacute bacterial endocarditis but other endocarditic and septic infections may cause purpura

5 Another class of purpura is the allergic or anaphylactoid type This includes Schonlein s where joint swelling pain and purpura are seen and Henoch s associated with abdominal pain and purpura

The pathogenesis of the secondary type of purpura is frequently obscure The purpuric eruption is not always brought on by the same mechanism The factors concerned in the development of petechial hemorrhages are

1 Defective production of platelets by the bone marrow

2 It has been postulated that the spleen produces an inhibitory substance which impairs the formation of platelets

3 A damaged capillary endothelium may be a factor In most cases of secondary purpura the chief changes are probably produced by increased permeability of the capillary wall plus thrombocytopenia as an added factor

4 Aplastic anemia pernicious anemia leukemia and myelophthisic anemia

5 The possible role of allergy and drug sensitivity must always be kept in mind

Signs and Symptoms The characteristic clinical picture as seen in purpuras of the essential or primary type is often lacking in the secondary group While purpuric spots occur in the skin and there may be bleeding from the gums and other parts of the body, the changes in clot retraction time and in the platelet count are not as prominent as in the primary form The associated underlying disease usually dominates the clinical picture so completely that the purpura seems to play only a minor rôle

Diagnosis Obviously the manifestations of the purpura are determined by the mechanism that causes it for example if the purpura is due predominantly to capillary damage the features will be different than if it is produced by defective formation of platelets

TREATMENT

The treatment of secondary purpura consists in treating the associated disease and cause

1 During the acute stage the patient should rest in bed have good nursing care and an appetizing well balanced diet Good results have been reported following the use of vitamin C 25 to 50 mg doses three times a day

2 Blood transfusions are often important especially if there is a disturbance of the platelet formation Small transfusions repeated every two or three days are better than large amounts as platelets are then furnished repeatedly and the life of platelets is very brief Subcutaneous or intramuscular injections of whole blood 20 cc every day or every other day have been found to be of benefit The favorable influence of such injections may be due to a foreign protein reaction

3 Intramuscular injections of liver extract 3 to 5 cc weekly are recommended Iron in the form of iron and ammonium citrate 2 Gm (30 grains) three times a day may be given

4 Calcium lactate 0 66 Gm (10 grains) every four hours or calcium gluconate 1 Gm (15 grains) intravenously every day have also been suggested

5 Rutin 10 to 20 mg three times a day or hesperidin 50 100 mg one to four times daily will control the purpura of certain individuals

6 Protamine 2 5 mg per kilogram of body weight has been found to be very helpful in some cases

7 Splenectomy is hardly ever indicated in secondary purpura

BANTI S DISEASE

Banti s disease or splenic anemia is a chronic disease characterized by splenomegaly anemia leukopenia a tendency toward gastric hemorrhage and an increase in the formation and destruction of blood cells In the later stages there is cirrhosis of the liver with ascites and jaundice The acute episodes in the chronic course constitute emergencies

Etiology The cause of Banti s disease is not known Some investigators question whether it is a distinct entity from the pathological point of view and claim that it is only a phase or period in some form of cirrhosis of the liver These men believe that some toxin or infection leads to cirrhosis of the liver and also to changes in the spleen There are however some distinguishing characteristics of Banti s disease not found in the average case of liver cirrhosis Most liver cirrhoses do not develop leukopenia anemia hematemesis and splenomegaly though it may be that certain types of cirrhoses of the liver are associated with these changes Banti s disease often comes on

in young people and that is one reason why it should be separated from real cirrhosis of the liver If all cases of Banti s disease were seen in the cirrhotic period (past 45 years of age) it would seem more likely that cirrhosis and Banti s were one and the same When it appears in younger individuals it is often confused with ulcer because of hematemesis or with other forms of blood dyscrasias because of the anemia and leukopenia

Pathology Histologically Banti described what is known as fibrosis of the malpighian corpuscles in addition to fibrosis of the trabeculae of the spleen He based the diagnosis of Banti s disease on these peculiar findings Some investigators believe that the disease is distinguished by these features others believe that these changes may occur during the course of ordinary cirrhosis of the liver

Signs and Symptoms Banti s disease has some very special clinical features It is a disorder that usually begins in youth and runs a course that covers over one half the period of an average life time The disease may be divided as Banti pointed out into three stages

1 The first stage begins early in life—in childhood or adolescence Anemia weakness leukopenia splenomegaly and frequently hemorrhage from the stomach occur The hemorrhage from the stomach is not produced by portal obstruction in the early stage The first stage covers a period of approximately ten years and is often called splenic anemia

2 The second stage ensues after ten years and is a period characterized by enlargement of the liver pallor more severe anemia greater enlargement of the spleen and frequently hematemesis This period covers a space of about two or three years

3 The third stage of this disorder is distinguished particularly by cirrhosis of the liver portal obstruction and the other signs and symptoms of Banti s disease—splenomegaly hematemesis severe anemia and leukopenia

Differential Diagnosis The diagnosis is decided mainly by exclusion A half dozen or more disorders may have to be excluded of which the first to be eliminated are carcinoma or ulcers of the stomach Next blood diseases typified by enlargement of the spleen such as Hodgkin s disease Gaucher s disease or Osler s disease must be considered The leukemias must be carefully differentiated from

Banti s disease During certain periods of the leukemic state the patient may have leukopenia Leukemia is associated with the presence of many pathological young cells—myeloblasts etc If one takes a careful history and is able to satisfy the four or five main features of Banti s disease as pointed out above there should be little or no difficulty in the differential diagnosis

Prognosis These patients usually live almost an average lifetime Hematemesis is the most serious complication that develops The disease itself does not produce a fatal outcome but life may be threatened by severe hemorrhage or by intercurrent infections Spontaneous recovery is unknown

TREATMENT

The treatment is largely dependent on the stage of the disease in which the patient is seen In the early stages when anemia and leukopenia are the characteristic features splenectomy is said to do good When gastric disturbances ascites and hematemesis predominate splenectomy is of no avail because these symptoms are produced by the cirrhotic condition of the liver The problem that often arises is the care of a patient with hematemesis The treatment should be the same as it is for hematemesis from any other cause

1 Complete rest
2 A protein diet with supplementary amounts of vitamins
3 Transfusions
4 Intravenous glucose in saline
5 Morphine in order to keep the patient quiet
6 Finally it is said that cod liver oil or haliver oil is of value

GAUCHER S DISEASE

Gaucher s disease which was first described by Gaucher in 1882 is a form of splenomegaly accompanied by hepatomegaly secondary anemia and leukopenia The theoretical aspects of this disease are probably more interesting and important than the clinical

Etiology There are a familial tendency and a preponderance of Hebrews in the reported cases The disease is characterized by hyperplasia of the endothelial or reticulum cells and the cause is now believed to be due to a hereditary disturbance of lipoid metabolism

Pathology The most distinctive finding is an enormous enlarge

ment of the spleen characterized by scattered white spots over the sur face which cells are filled with lipoid It is the swelling of these cells that causes the increase in size of the spleen The liver lymph nodes bone marrow and other parts of the reticuloendothelial system may also be involved

Signs and Symptoms Gaucher s disease is characterized by the constant signs of splenomegaly Hepatomegaly secondary ane mia and leukopenia are present as the inconstant features of a tend ency toward bleeding of the nose and gums brownish yellow dis coloration of the skin and paracorneal wedge shaped conjunctival thickenings Occasionally there are gross and radiologic long bone changes consisting of palpable thickening angular deformity of the spine and pathological fractures The x rays show thinning of the cortex expansion and widening of the medulla and a mottled ap pearance of the long bones

The peripheral blood picture is not striking but the presence of splenomegaly hepatomegaly mild secondary anemia leukopenia of 3000 to 6000 with reduced polymorphonuclears relative lymphocy tosis and unaltered monocytes and thrombocytopenia of the order of 125 000 should lead one to suspect the disease

Diagnosis Definite and indisputable diagnosis is made by study ing smears of aspirations of the spleen or bone marrow which typi cally contain the Gaucher cell These cells are of extreme size ranging from 40 to 60 micra in diameter their nuclei stain darkly and are eccentrically placed the cytoplasm is clear and contains fine fibrillae coursing parallel to the long axis of the cell It is now known that these cells are elements of the reticuloendothelial system impreg nated with a product of disturbed lipoid metabolism in combination with a protein to form a cerebroside

The condition may have to be differentiated from Banti s disease and hemolytic jaundice Gaucher s disease may be excluded if portal cirrhosis and ascites are found as these are not features of Gaucher s disease early in the disease however it may not be possible to dis tinguish them clinically unless gastric hemorrhage occurs to clarify the picture Hemolytic jaundice offers no difficulty if the familial relationship the icterus and the blood picture of nucleated red cells with 10 to 20 per cent reticulocytes and increased red cell fragility are appreciated

Prognosis Patients with Gaucher s disease have been known to live 40 years with the condition Infant mortality however is high and prognosis is bad in all cases where a neurological involvement is present

TREATMENT

Splenectomy is the only known measure that can alter the course of Gaucher s disease Since this procedure is dangerous and as a rule merely slows the process it should be practiced with reserve Cure is hardly to be expected as the disease progressively involves more of the reticuloendothelial elements in the liver bone marrow and lymphatic tissue until death ensues during the late twenties or early thirties However if the operation is successful improvement may be expected and if progress outside the spleen is slow enough the improvement may be permanent

POLYCYTHEMIA VERA

Polycythemia vera is a rare disease also known by the synonyms polycythemia rubra vera erythremia splenomegalic polycythemia Vaquez s disease and Osler s disease Though the chronic condition progresses slowly and eventually ends in death the acute exacerbations require prompt and skillful medical attention Polycythemia vera is characterized by excessive formation of erythroblasts by the bone marrow This results in persistent polycythemia with splenomegaly which gives a red cyanotic appearance to the skin and causes erythrosis increased viscosity and volume to the blood and distention and engorgement of the capillary vessels

Etiology Although the cause of polycythemia vera is obscure it is believed that heredity may have some bearing on the incidence of this disease Local anoxemia of the bone marrow may also play a part as the level of the red cell count is controlled by the oxygen tension of the bone marrow

Males are said to be more commonly affected than females and the disease is known to have a high incidence in Jews The age of onset occurs most frequently in middle life

Pathology The pathological changes consist of hyperplasia of the red cells This causes an increase in the amount of red bone marrow which replaces the normal yellow marrow Most important

of all is the decided increase of total blood volume as well as the increase in number of red cells to over 6 000 000 per cmm

Signs and Symptoms The clinical picture is characterized by a most varied number of syndromes One or another may dominate the clinical picture for a time then disappear and either return at a later date or never return at all The changes which occur in the different body systems may be summarized as follows

1 Brain and nervous system
   a Dizziness
   b Headache
   c Lapses of memory
   d Complete change of personality Individuals who have been happy may become irritable frugal people become spendthrifts a man who has been happy in his family life may start going about with women
2 Cardiovascular system
   a Palpitation of the heart
   b Flushing of the hands and face
   c Drumming in the ears
   d Pulsation in the wrists
   e Cyanosis or redness of face and neck.
   f Hypertension
3 Respiratory system
   a Coughing
   b Hemoptysis
   c Dyspnea
   d Pain in the chest
4 Gastrointestinal system
   a Nausea and vomiting
   b Diarrhea
   c Vomiting of blood
   d Enlarged liver and spleen
5 Urinary tract
   a Albuminuria.
   b Blood in the urine
   c Frequency of urination
6 Vascular diseases of the extremities (these are of great importance)
   a Thrombotic lesions in the arteries
   b Functional occlusion of vessels with blocking of flow of blood leading to ischemia and gangrene of the feet simulating Buerger s disease
7 Change in blood
   a Darkness of color
   b From 7 000 000 to 12 000 000 red blood cells per cmm (up to 6 000 000 is not considered polycythemia)

c Hemoglobin values of from 18 to 24 Gm per 100 cc. blood
d Normal individual red corpuscles
e Increase of blood platelets
f Increase of total blood volume
g *Hyperplasia of all marrow elements*
h Leukocytosis

Differential Diagnosis In association with the patient s appear ance and splenomegaly *the most important clue to diagnosis is per* sistent absolute polycythemia not connected with any cause In addition there is increased erythrogenesis associated leukocytosis and thrombocytosis which help in distinguishing erythremia from erythrocytosis *Diagnosis of polycythemia vera should not be made* unless the red blood count is over 6 000 000 If this rule is followed one will not confuse erythremia with an increase of red cells due to living at high altitudes and administration of certain drugs or *poisons or vasomotor instability* The *gastrointestinal symptoms and* those referrable to the central nervous system heart kidneys and *sense organs must not be confused with symptoms of local primary* disease

Prognosis *Polycythemia is a chronic condition with spontaneous* prolonged remissions and acute episodes After the onset of the first symptoms the patient may expect to live from 4 to 20 years The disease is fatal in the long run though death may be brought on by *other causes* The *patient may die during an exacerbation of the dis* order from thrombosis or hemorrhage Modern methods of treat ment have improved the prognosis somewhat

TREATMENT

Venesection is by far the most important method of treatment for polycythemia vera because there not only is a great increase in blood volume but also in the number of red blood cells The hematocrit *reading is* decidedly increased and the hematocrit may be taken as a guide for venesection At first venesection must be done every week or ten days then it may gradually be diminished to once every month In time it has to be done only occasionally as the condition *of the* patient requires it Amounts of 400 to 500 cc are withdrawn

Phenylhydrazine hydrochloride is said to be beneficial Two tenths of a gram (3 grains) is given daily for three or four days

then 0 1 Gm (1½ grains) is administered daily until the leukocytes increase or the hemoglobin falls below 100 per cent After this happens 0 1 Gm (1½ grains) is given every second or third day, or medication may be discontinued until the leukocytes begin to fall or the hemoglobin begins to rise The periods between medication are gradually lengthened in the hope that the blood hemoglobin and leukocyte count can be stabilized by 0 1 Gm (1½ grain) doses given once a week

It has been thought that liver injury may result from this type of therapy but this has not been proved The blood should be carefully studied during the course of treatment in order to avoid unfavorable responses Giffin and Conner feel that the patient should be kept ambulatory as much as possible that patients confined to bed should not take the drug and that this drug should be used with extreme caution in the cases of patients over 60 years of age

Acetylphenylhydrazine is considered superior to phenylhydrazine hydrochloride since it is less toxic and the dosage easier to regulate The dose is 0 1 Gm (1½ grains) given every day for two or three days then medication is stopped for a few days a blood count taken and treatment resumed This procedure is followed for three or four weeks when the dose may be increased to four five or six doses per week if that is necessary If there is any drop in hemoglobin or erythrocytes the drug is stopped at once for a week or longer Great care must be taken to adapt the dosage to the patient as individual tolerance varies greatly Signs of overmedication are drop in red cell count jaundice gastrointestinal symptoms and fever

Saturation with Fowler s solution in the usual way is helpful The best result from this treatment is effected if the patients reach a 20 minim dosage three times daily instead of stopping at 10 minims

Although roentgen therapy of the spleen is harmful irradiation of the long bones is good Rather large doses are given to the long bones sternum scapula vertebra ribs and pelvis The effect is temporary and therapy must be withheld if decrease in the leukocytes of the circulating blood indicates impairment of the leukocyte forming mechanism in the narrow The disadvantage of this form of treatment is that it is not immediate in effect and one is not sure whether it is helping the patient or doing harm Spray irradiation

therapy is also a form of treatment used for polycythemia vera but as yet its long term effects cannot be predicted

Recently radioactive phosphorus has been used in treatment with good results From 4 to 7 mc intravenously is administered as an initial dose Second and third doses are given after an interval of a week or two This treatment is not curative but remissions lasting from 9 months to 2 years have been reported

Nitrogen mustard given intravenously has been found to cause remissions in some cases

CHAPTER IV

The Heart

The routine medical practice is apt to lull one into a sense of self sufficiency to a degree that the physician fails to be prepared for the acute emergency which is sure to come sooner or later When this acute episode develops the judgment and skill of the practitioner are tested to the utmost for upon proper diagnosis and prompt and skillful management the life of the patient depends

Of the many kinds of acute emergencies none is more dramatic or important than that associated with diseases of the cardiovascular system While the chronic diseases of the heart and circulatory system are usually easily diagnosed and treated the acute events that develop primarily or in the course of the chronic ailment may find the resourcefulness of the physician lacking The types of so-called cardiac emergencies met with in both hospital and general practice are those associated with (1) the coronary arteries (2) right and left ventricular heart failure (3) the arrhythmias (4) embolism and thrombosis and (5) hypertensive cerebral vascular crisis

DISEASES OF THE CORONARY ARTERIES

There are two main clinical manifestations of coronary artery disease While these are usually treated as distinct clinical entities it would be as correct to consider them under one heading and describe the chief events as different stages of the same disease For the purpose of this chapter these two conditions will be described separately They are (a) angina pectoris and (b) coronary thrombosis Since diseases of the coronary arteries usually develop on the basis of an arteriosclerotic lesion it is rare to find this class of heart disease in individuals under the age of 40 years But by the same token most people over the age of 40 years sooner or later develop some sclerosis of the coronary branches

Angina Pectoris

Angina pectoris is a term over which considerable difficulty has arisen Many authorities believe it is so inaccurate that it should be

dropped while others advocate its use In my opinion, it is a very satisfactory term if one uses it in its proper sense Angina pectoris is a name indicating a particular kind of pain in the chest due to interference with the proper blood supply to the heart muscle *If one uses the term loosely to designate a variety of chest pains which* have nothing to do with the heart or circulatory *system* then confusion arises and the term becomes more of a nuisance than a help in diagnosis The term will be used here strictly for the type of pain that comes when the coronary arteries are involved If this is done

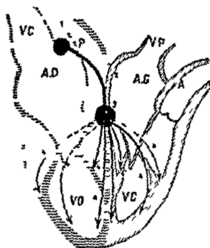


Fig 1—Diagram of the bundle which transmits the neuro myocardial stimuli (bundle of His) V C vena cava V P pulmonary vein P pulmonary artery A aorta A D right auricle A G left auricle V D right ventricle V G left ventricle 1 and 2 sinoauricular node 3 auriculoventricular nucleus 4 4 terminal neuromyocardial ramifications of the bundle

then as a rule the characteristics of angina pectoris are fairly clear The term status anginosus is applied to a clinical condition in which the pain is of greater duration than the pain of angina pectoris lasting for an hour or two or longer It is a form of coronary insufficiency and evidences of myocardial infarction are slight

Etiology In the past many theories have been advanced for the explanation of angina pectoris The idea that hardening of the coronary arteries was the chief cause of the angina came from Edward Jenner, *but this theory was not established as a fact and such hy*potheses as aortitis and coronary spasm were advanced to explain the pain Our modern conception of anginal pain is based to a large

extent upon the work of Thomas Lewis who showed by analogy with the muscular pain of intermittent claudication to angina pectoris that the pain is due to a relative insufficiency of the blood supply to the heart muscle He pointed out too that the pain of angina pectoris where the blood supply to the heart muscle is not completely shut

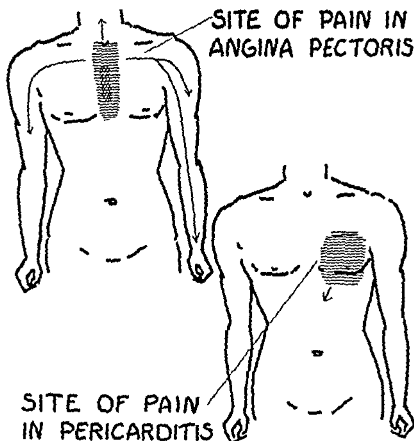


Fig 2

off is the same kind as that in coronary thrombosis where complete occlusion of an arterial branch blocks off the blood supply entirely The difference is that in the spasmodic type of pain the insufficiency is partial while in the other it is complete and the pain is not relieved within a period of from five to ten minutes but continues on with greater severity for hours or sometimes days

Recently a new conception of angina has arisen which tends to show that anginal *pain seems to be due to excessive activity in the* vasodilator pain fibers in the posterior nerve roots passing to the mediastinal structures and the coronary vessels This is not necessarily caused by anoxia

The male sex is affected almost three times as often as females and most patients having this disease exceed 40 years of age There is a high incidence in Jews Negroes are almost always exempt

Pathology *Many theories have been advanced to explain the* pathology of angina pectoris The originator of the term Heberden believed that the coronary arteries were hardened and narrowed Following Heberden s time this term was used for almost any type of chest pain and the relationship of the coronary system and angina pectoris was lost Such terms as spurious angina false angina angina notha and pseudoangina pectoris all came into use to describe certain sensations in the chest associated with assumed or genuine lesions of the heart The state of confusion existed until about 1912 when Herrick first described coronary thrombosis as a separate clinical pathological entity By a gradual process angina pectoris and coronary *thrombosis* were seen to merge as different syndromes in the course of the same disease Although I must emphasize that certain cases occur apart from organic disease of the coronary system and are explained on the functional basis as a coronary spasm clinically and at autopsy these are too rare to be of any great consequence in practice However many of these cases are the result of an ischemia of the heart muscle caused by anemia tachy*cardia or hypotension*

Signs and Symptoms Angina pectoris is distinguished by the following three factors

1 Pain under the upper portion of the sternum

2 The radiation of the pain down the left arm up the left side of the neck and sometimes in both arms

3 An emotional element is usually an outstanding mark This *consists* of a sensation of fear that something disastrous is going to take place

The painful sensation is often difficult for the patient to describe and more difficult for the physician to interpret This distressful feature seldom is *a sharp lancinating type of pain* but more often

consists of a tightness as if a band is about the upper part of the chest Sometimes the patient feels he is suffocating This pain is usually most marked over the upper portion of the sternum

The attack of angina pectoris comes on as a rule following any one of three events (a) Exercise (b) emotional strain or (c) a heavy meal The attack is usually sudden at onset lasts from five to ten minutes and then disappears promptly and completely with out aftermath There is no evidence of cardiovascular shock and the heart sounds force and rhythm may be as good after the attack as before Cyanosis dyspnea and other evidences of heart failure are lacking The blood pressure may rise during the attack but usually returns to normal following the attack After the spell is over the patient feels as well as before and only hopes that a recurrence will never take place The earlier attacks are usually mild but as time advances these spells become more frequent and more prolonged Finally one comes but does not disappear like the others It fails to respond to the simple treatment the patient has taken for relief before and suddenly it dawns on the patient that something more has happened than a mere angina attack The clutching in his chest is more severe the tightness is greater and he is weaker than ever before He feels his heart thumping and beating irregularly and he falls over in collapse

It is evident that the coronary system which for several months to several years has demonstrated its ability to furnish the proper amount of blood to the heart muscle in angina pectoris has finally suffered from an acute occlusion of one of its main branches by a thrombus The patient then no longer has simple angina pectoris but a more disastrous kind of coronary disease — namely coronary thrombosis Angina pectoris however does not always end up with coronary thrombosis Coronary disease that produces angina pectoris may lead to myocardial degeneration and fibrosis with auricular fi brillation and failure of the heart muscle On the other hand the patient may overcome the angina pectoris and after several years of frequent struggles with these painful attacks may never suffer from them again

Diagnosis While the diagnosis of angina pectoris is not always easy if one keeps in mind the essential features as the age of the patient the nature of the onset of the first sign of distress and the

periodicity of the course associated with the main causes of the dis ease then it becomes comparatively simple The electrocardiograph is about the only instrument of precision that may aid in diagnosis and temporary reversible changes in the T wave and ST segment in one or more of the standard limb or precordial leads may be ob served during the attack or carefully controlled provocative tests At times however electrocardiography proves of little value as the findings may be negative The old adage Listen carefully to what the patient says and he will tell you the diagnosis is appropriate here

The differential diagnosis of angina pectoris is difficult because so many conditions apart from the heart and coronary arteries may produce a pain that in a faint way simulates it as pleurisy aortitis arthritis of the sternocostal joints intercostal neuralgia and gallblad der disease The differential diagnosis is made easier if one insists upon a careful history of the course of events remembering that periodic attacks of angina pectoris have a clocklike regularity and disappear by themselves within a short period or with the aid of nitro glycerin amyl nitrite or other vasodilators Such treatment will have absolutely no influence on the course of other diseases confused with angina pectoris

Prognosis Prognosis in angina pectoris varies with the amount of involvement of the heart and the frequency of attacks Usually the highest mortality rates occur in the first year following diagnosis and decrease each year The 5 year survival rate observed in a statistical study of 3440 patients examined at the Mayo Clinic by Parker and *others was 53 2 per cent*

TREATMENT

Angina pectoris is a condition that calls for ambulatory treatment rather than bed rest which is required in coronary thrombosis The regime of management of angina pectoris is as follows

1 The patient with angina pectoris must be educated to live within the rigid boundaries set up by his disease and shorter hours more leisure and freedom from emotional strain are the main ther apeutic factors In addition anything that causes the patient distress should be avoided such as gas producing food tobacco and abuse of the use of alcohol Notwithstanding a variety of opinions upon the

benignity or injuriousness of nicotine in angina pectoris these patients are better off without tobacco While the effect of alcoholic drinks on these patients is somewhat debatable a limited amount of whiskey brandy or other strong liquor may be well borne and in some cases may even do good

An exciting cause or a trigger factor should be sought in every case These include gallbladder disease peptic ulcer and hiatus hernia any of which may precipitate an anginal syndrome in an otherwise subclinical coronary sclerosis

2 The attack may be relieved by 0 65 mg (1/100 grain) of nitroglycerin This tablet should be placed under the tongue and allowed to melt Relief is experienced within 2 or 3 minutes If faster results are required an amyl nitrite pearl may be placed in a handkerchief and broken the inhalation from the pearl usually bringing about prompt relief from the pain in approximately 30 seconds Longer acting nitrates such as erythrol tetranitrate or mannitol hexanitrate 1/2 to 1 grain (30 to 60 mg) every 4 to 6 hours have also been used to decrease the frequency of the attacks

3 Between periods of severely painful episodes various sedatives as elixir of bromide or phenobarbital one teaspoonful may be given four or five times a day to control the excitable nervous system

4 Drugs of the xanthine group are often used effectively over a long period of time Theobromine 0 3 Gm (5 grains) or aminophylline 0 2 Gm (3 grains) with 0 03 Gm (1/2 grain) of phenobarbital may be given three times a day These drugs are said to increase the blood flow in the coronary system and promote better nourishment of the heart muscle However vasodilating drugs may not always do good When there are rigid ostia or segments in the main coronary vessels these drugs will not effect coronary vasodilatation However they may relax the reflex spasm of the collateral vessels The drugs cause dilatation not only of the coronary vessels but also of the peripheral vessels which tends to prevent the return flow to the heart This may be followed by anoxia or reduced oxygen supply to an already damaged heart Vasodilating drugs when incorrectly used may cause myocardial infarction

5 Papaverine hydrochloride may bring about improvement It should be given in doses of 0 1 Gm (1 1/4 grains) in tablets four times daily over a period of time It has been considered good to

alternate two weeks of papaverine medication with two weeks of *placebo medication* Papaverine may also be given intravenously in large doses with a wide margin of safety The writer has used with good success 3 grains (0 2 Gm) intravenously and has repeated this dose three or four times a day Its action is that of a mild sedative and a definite and prolonged coronary vasodilator It is not very toxic, and is not a myocardial depressant This drug is contra indicated only for intravenous administration in complete auriculo-ventricular block

6 The frequency severity and duration of attacks may be reduced and exercise tolerance increased in some individuals by therapy with testosterone propionate 25 mg (0 4 grain) every fifth day for a total of 5 to 25 injections The average number of injec tions needed is 11 Improvement is not immediate as with nitro glycerin since about 28 days pass before quantitative improvement *is noted and about 43 days before it is marked During therapy* blood pressure is usually lowered

7 Intravenous infusions of 50 to 200 mg of nicotinic acid during a period of about 3 weeks or the oral administration of the drug 25 mg three times a day have brought about prolonged subjective and objective betterment and may reduce both blood pressure and heart rate It is thought that nicotinic acid causes a rise of pressure to the brain and an increased blood supply to the brain accompanied by inverse changes in the rest of the body

8 The use of an elastic abdominal support may prevent anginal attacks

9 In selected instances of intractable angina pectoris that do not respond to any form of therapy the use of propylthiouracil (150 to 200 mg) daily has been suggested If the metabolic rate falls too low the dose is later reduced to 50 mg daily However one must guard against myxedema after prolonged use and against the occur rence of reactions particularly agranulocytosis because of its seriousness

10 *When medical measures prove inadequate* the following surgical measures must be considered Chemical destruction of the sympathetic nerve ganglia and their rami sympathetic ganglionec tomy or posterior rhizotomy

Coronary Occlusion Thrombosis and Insufficiency

In discussing diseases of the coronary arteries confusion has arisen in terminology because of the interchangeable use of the words coronary occlusion coronary thrombosis and coronary insufficiency While there is no complete unanimity of opinion concerning the preferred use of these terms the following interpretation seems justified For practical purposes coronary thrombosis and coronary occlusion may be used interchangeably but coronary occlusion is favored Complete occlusion of a coronary artery may occur without thrombosis as the partially occluded artery may become completely plugged by hemorrhage into the intima or by conditions other than thrombosis Myocardial infarction may develop without complete coronary occlusion or thrombosis and coronary occlusion may occur without myocardial infarction if the development of the process is slow and collateral circulation becomes well established

The term acute coronary insufficiency however should be differentiated from coronary occlusion and thrombosis both clinically and electrocardiographically One of the chief clinical differences between the two is the abruptness of onset of coronary occlusion and the more insidious development of coronary insufficiency Another difference is that a number of factors such as trauma shock exertion and excitement influence the onset of acute insufficiency while acute thrombosis or occlusion often occur during rest or sleep The area of infarction in occlusion or thrombosis is frequently large extending from the endocardium through to the pericardium and it is more often fatal than an attack of insufficiency where the area of infarction is apt to be small and not confluent and is restricted to the subendocardium

Coronary Occlusion and Thrombosis Acute coronary occlusion is one of the most dramatic and disastrous events encountered in the practice of medicine Approximately 30 per cent of these patients die within 24 hours after the onset of the attack 45 per cent recover partially but remain cardiac invalids only to succumb to heart failure another coronary attack or some other intercurrent disease within a period of five years and approximately 25 per cent recover completely Prompt and accurate diagnosis is of first importance

for frequently a surgical condition of the abdomen may be confused with coronary thrombosis If one operates upon an individual with a coronary attack with the idea of relieving an acute abdominal dis ease as perforation of a viscus which is not present the patient rarely survives On the other hand failure to operate when there is an acute abdominal condition may lead to the patient s death

Etiology and Pathology The cause of coronary occlusion is usually a thrombus on the base of an atherosclerotic plaque Em bolism is seldom the cause of obstruction

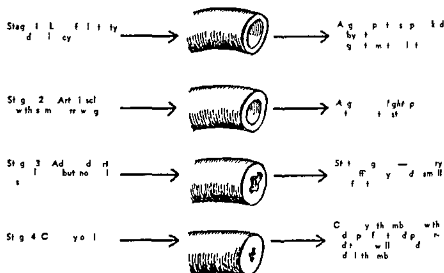


Fig 3—Correlation of coronary disorders and the clinical features

The patient with angina pectoris is always a candidate for coronary thrombosis and the fundamental basic lesion of arteriosclerosis is the same in both angina pectoris and coronary occlusion The par tially occluded coronary vessel of angina pectoris becomes completely shut off by the development of a coronary artery thrombus *This* must not be taken to mean that angina pectoris always precedes an attack of coronary thrombosis because the thrombostatic episode may occur abruptly without any preceding evidence of any kind of cardiac disturbance

Signs and Symptoms As in angina pectoris exercise emotional strain or a heavy meal may precipitate the attack but it is well

known that the attack may come on independent of any one of these conditions occurring while the patient is sleeping It usually begins with a sudden pain in the region of the sternum or in the epigastric area Because of the location of the pain in the abdomen so-called acute indigestion or gallstone colic may be suspected The pain may simulate that of a preceding attack of angina but it differs in that it fails to be relieved by rest or nitroglycerin within the usual period of about ten minutes This pain continues and then the asso

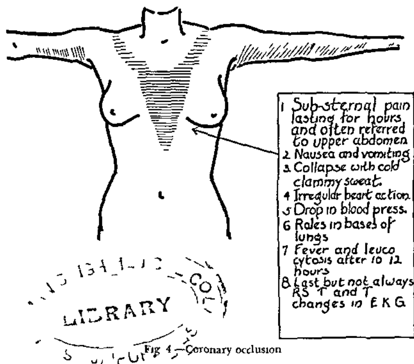


Fig 4 —Coronary occlusion

ciated phenomena characteristic of coronary thrombosis set in with weakness sweating nausea and vomiting palpitation and irregularity of heart action and the patient may collapse

Diagnosis Differential diagnosis is more important today than ever before because the treatment of coronary disease has become more painstaking exact and effective Furthermore since coronary thrombosis is simulated by acute abdominal emergencies it is obvious that certainty in diagnosis may be a matter of the patient s life or death Coronary disease may be confused with certain surgical emer

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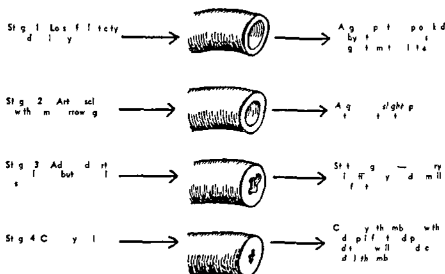


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with substernal oppression some with pain but no collapse and others with pain but no dyspnea

b *Palpation* When one takes the radial pulse he finds it weak rapid and sometimes intermittent Palpation further reveals that the patient is covered with a cold clammy sweat On placing the hand over the heart area irregular action may be felt If the blood pressure is taken at this point it is found though not invariably so to have dropped well below a normal level

c *Auscultation* The heart sounds are not clear and normal but on the contrary are muffled rapid and often there is an irregularity I must emphasize though that there may be no signs of heart disease in the earlier periods of the attack but they may come hours later Fever leukocytosis and pericardial friction may also appear and help cor roborate the diagnosis

Usually an electrocardiographic examination is unnecessary in outspoken cases In the less severe forms of the disease when other conditions may simulate it the electrocardiogram plays an impor tant part However as far as the acute emergency goes laboratory aids are unnecessary in diagnosis though they are useful

Differential Diagnosis It was stated above that the pain of coronary obstruction may occur in the abdomen and simulate acute abdominal emergencies There are several diagnostic points to be remembered when the differentiation between true coronary disease and an abdominal catastrophe is made

1 As a general rule the pain of coronary disease is mainly above the nipple line while usually the pain of an abdominal catastrophe is below the nipple line

2 The pain of an acute coronary thrombosis may occur in the abdomen but it does not become localized nor does it correspond to the pain of one of the essential organs For example pain of gall bladder disease may be in the epigastric area but tenderness will be localized over the gallbladder area There is no localized area of tenderness in the referred pain of coronary disease

3 With coronary disease there may be marked distention of the abdomen but rigidity of the abdominal wall as that seen in per foration of an ulcer is lacking In abdominal catastrophes the patient usually is content to lie flat on his back in bed and remain as quiet as possible while in coronary disease the patient usually tosses and turns and is restless

4 In coronary disease the veins of the neck may be full and

gencies particularly with acute perforation of peptic ulcer gallstone colic acute *hemorrhagic pancreatitis and bowel obstruction* Intra thoracic conditions or diseases may also cause confusion in diagnosis The more important are Pneumothorax massive collapse of the lung pulmonary embolism hiatus hernia dissecting aneurysm of the thoracic aorta acute pericarditis and lobar pneumonia Paroxysmal tachycardia paroxysmal auricular fibrillation and flutter may also resemble coronary occlusion

Several important features must be kept in mind for the purpose of differentiation

1 A primary requisite is an accurate history of just how the attack began and what preceded it Sometimes it is not possible to obtain this information *The pain may be too severe or the patient* may be in shock or a state of collapse but in most instances this information is available if one tries hard enough to obtain it A history of former episodes of angina like pain of hypertension or of irregular heart action may cause one to concentrate on coronary disease while a history of pain relieved by food or alkalies may lead one to think of a peptic ulcer A story of repeated attacks of pain in the abdomen with vomiting fear of eating fatty food cauliflower or cabbage should lead one to consider gallstones as a likely disease The sex and age of the patient must be borne in mind since coronary thrombosis occurs seven times as often in men as in women and it is a disease of middle life and after

2 Examination

a Inspection When one is called to see a patient who has had a sudden attack of some kind coronary disease is usually foremost in one s mind particularly if the patient is a man beyond middle age On inspection the individual appears to be in great difficulty He *is apt to have a deathlike expression on his face and the peculiar* grayish cyanotic tinge of the skin confirms one s suspicions It is apparent that the patient has had a knockout blow of some kind few if any diseases leave an individual in such a miserable prostrated condition on such short notice The fingernails are usually cyanotic breathing is difficult the patient is restless He often assumes first one position then another and yet another in an effort to obtain freedom from the cramp *strangling or oppression which* has developed With increasing frequency we are recognizing symptomatically milder forms of coronary disease some with no pain but

with substernal oppression some with pain but no collapse and others with pain but no dyspnea

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4 In coronary disease the veins of the neck may be full and

distended but in surgical conditions of the abdomen the patient is usually pale and appears pasty and bloodless

5 Evidences of impaired circulation as dyspnea cyanosis and cough are absent in abdominal emergencies

6 On auscultation considerable evidence of great importance is obtained In the coronary attack the heart and circulatory system usually show evidences of grave injury and examination of the bases of the lungs may reveal many rales due to pulmonary congestion

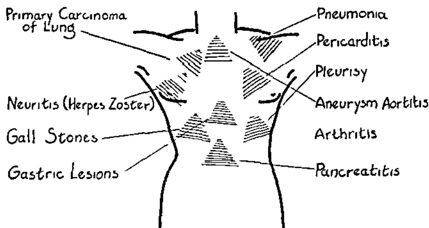


Fig 5—Conditions simulating coronary artery disease and the location of most tender area in the respective conditions

Congestion may be so marked that the patient coughs up a pinkish frothy foamy material characteristic of edema of the lungs But auscultation is too often limited to the chest If one examines the abdomen with a stethoscope too valuable information is obtained In coronary disease the abdomen is soft and normal intestinal gurgles are usually present while if the condition is due to intra abdominal catastrophe intestinal gurgles are apt to be entirely absent and the wall of the abdomen is firm and rigid

Other diseases than those of the abdomen must be kept in mind when one is considering the differential diagnosis of coronary thrombosis Diseases of the chest must be considered Of these the following are most important *because they like coronary disease may* be distinguished chiefly by pain in the anterior chest Fibrinous pleurisy, early pneumonia acute pericarditis aortitis dissecting

aneurysm arthritis involving the sternocostal joints, neuritis as herpes zoster and acute interstitial emphysema These diseases will be considered in their separate chapters and the features simulating coronary disease will be dwelt upon

TABLE I

	Angina Pectoris	*Coronary Occlusion*	*Gallbladder Colic*
Age	Over 40	Over 40	After adolescence
Sex	Male	Male	Mostly females
Cause of attack of pain	Effort	At rest	Gallstones
Onset	Sudden sternal pain	Sudden sternal pain	Without effort
Location of pain	Sternal	Sternal	Usually diffuse over lower chest or upper abdomen Finally localized over affected organ
Duration of pain	Minutes	Hours	Many hours
Condition between attacks	No distress	Heart trouble	Pain usually persistent
Shock	Absent	Present	Unlikely
Blood pressure	Raised	Lowered	Inclined to be low
Heart sounds	Unchanged	Gallop irregular	Rapid but otherwise normal
Dyspnea	Absent	Present	Absent
Cyanosis	Absent	Present	Absent
Congestion	Absent	Present	Absent
Fever and leukocytosis	Absent	Present	Always some abnormality
Electrocardiogram	Changes often present	Typical changes present	Nothing significant

The painful syndrome of coronary disease may be confused with disorders below the diaphragm The following table emphasizes the chief points to be remembered in differential diagnosis

The differentiation of coronary thrombosis from a multitude of other diseases in most instances requires only the diagnostic ability possessed by almost every practitioner I wish to emphasize however that some cases present problems of great difficulty For this minority I have the following advice to offer

1 As a rule the diagnosis is made by determining accurately and exactly the very first symptom and analyzing carefully the appearance and course of the associated phenomena In coronary disease pain is the first and most outstanding feature in practically all cases The two remaining members of the important triad of symptoms in coronary disease are dyspnea and vomiting

2 If one keeps in mind that in coronary thrombosis the heart muscle is profoundly injured and that the signs and symptoms will all tend to point towards a disordered cardiovascular system then usually the diagnosis will be properly made

3 When there is any decided difficulty in diagnosis and coronary thrombosis is a likely disease treat the case as one of coronary thrombosis As a rule the treatment will do the patient no harm provided the acute surgical abdomen has been ruled out

Prognosis Of many diseases where the future of the patient is unpredictable coronary thrombosis is the first on the list The patient with the most severe attack may recover completely while one with the mildest form may die suddenly The patient may live for a few minutes or go on to complete recovery and live a full life However the law of averages teaches that there is only one course to follow when the diagnosis is made and that is to set down a rigid set of rules for treatment and to follow them strictly

Acute Coronary Insufficiency Acute coronary insufficiency is characterized by coronary arteriosclerosis which causes a progressive narrowing of the arterial tree but at the same time retains functional capacity until some added factor precipitates functional inadequacy Added conditions which cause an increase in heart action are followed by an ischemic area in the heart The clinical picture is less startling than that of coronary occlusion because the onset is more gradual Angina pectoris dyspnea on exertion and distress after

meals frequently precede the myocardial infarct by some weeks or months The infarct is more limited and seldom causes the endocardial and pericardial lesions usually found in occlusion or thrombosis

Chest pain which is practically always present in occlusion is frequently absent and shock vomiting nausea, and a sharp fall in blood pressure are not common in insufficiency Fever leukocytosis and heart failure may come on gradually or never develop at all There may be a characteristic electrocardiographic pattern in occlusion and insufficiency In occlusion the electrocardiogram presents deep Q waves and RST elevations progressing into T wave inversions which persist for some time In insufficiency the electrocardiogram shows RST-depressions and T wave inversions which last several hours or days Master and his associates found the characteristic electrocardiographic pattern of coronary occlusion associated with occlusion at autopsy in 95 per cent of the cases

TREATMENT OF CORONARY OCCLUSION THROMBOSIS AND INSUFFICIENCY

There are 15 main points to be remembered in the treatment of coronary artery disease

1 The first thing to do when one is called to see a patient suffering from coronary thrombosis is to place the patient in the position that gives him the most comfort This is especially important because the patient may be too weak or sick to assume the posture that he wishes Except in cases where the patient suggests a different position one should lift the individual onto a backrest because most patients feel better when the head and chest are elevated

2 The patient with coronary thrombosis must be kept strictly in bed for some six weeks to two months There is no such thing as far as treatment goes as a minor attack If the diagnosis of coronary thrombosis is made treatment must be directed as if the attack were a major one

3 Since the patient usually is in great distress morphine or pantopon should be given at once I do not agree with many authors who advise large doses of morphine immediately for morphine although it is a great pain reliever may cause severe nausea and vomiting Pantopon in doses of 0 02 Gm (⅓ grain) is milder

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and kinder to the patient My practice is to give either pantopon 0 02 Gm (1/3 grain) or morphine 0 045 Gm (1/4 grain) with atropine 0 9 mg (1/70 grain) immediately and then if more narcotic is necessary these average doses may be repeated This seems a better practice than resorting to large doses immediately It is not necessary to relieve the patient s pain or distress with one bold therapeutic stroke it cannot be done and large doses of morphine as 46 or 64 mg (3/4 or 1 grain) as I have seen given at times may do more harm than good Atropine 0 9 mg (1/75 grain) may be given subcutaneously every four hours for eight doses

For the pain metopon a methyl derivative of dilaudid and demerol may be helpful Metopon does not depress the respiratory system as much as morphine it has greater analgesic power less tendency to induce addiction less emetic properties Demerol is given in doses of 50 to 100 mg orally or intravenously As a pain reliever it compares favorably with morphine has less tendency to adduce addiction and is less irritating to the gastrointestinal tract

4 If the patient is pulseless and in shock coramine 5 to 10 cc intravenously is often a lifesaving measure The use of plasma in amounts of approximately 250 cc given slowly intravenously as necessary has been recommended for this complication

5 A patient should not be moved immediately if he is in a state of collapse He should be treated where he is for a half hour or more before being moved to the hospital

6 Oxygen must be started and continued until the patient is out of danger

7 Aminophylline 0 52 Gm (8 grains) in 50 cc of 50 per cent glucose solution may be administered intravenously twice a day Sometimes aminophylline in combination with atropine and phenobarbital is best

8 Unless vomiting is pronounced dehydration need not be considered seriously Small amounts of fluid as 500 cc of five per cent glucose *solution may be given intravenously twice a day* but large doses, as 1000 cc or more are positively contraindicated because they throw an added burden on the heart and may cause failure

9 When food can be taken it should be liquid or semisolid easily digestible and given in small quantities Iced liquids are to be avoided When food cannot be taken by mouth or when there

is vomiting 50 cc of 25 per cent glucose solution may be given intravenously twice a day with 5 to 10 per cent glucose solution given by rectum through a Harris drip At the end of the second or third week solids may be added to the diet Vitamins should be provided

10 Alcohol given in small doses such as 15 to 30 cc several times daily may promote a feeling of well being if the patient has been used to taking alcohol before It should not be given with iced or charged water

11 Papaverine hydrochloride 09 Gm (1½ grains) intravenously and slowly may be given during the acute episode This may be continued in the dose of 06 Gm (1 grain) hypodermically every 24 hours If the patient is able to take the drug by mouth it can be given orally in the same dosage

12 Quinidine may be given in an initial test dose of 0 2 Gm (3 grains) and increased 1½ grains every 3 hours until a therapeutic effect has been obtained until evidence of toxicity has appeared or a maximal lump dose of 18 grains has been given Its prophylatic use when confronted by frequent ventricular premature beats has been advised in doses of 0 2 to 0 3 Gm (3 to 5 grains) every 4 hours The indicated precautions and electrocardiographic and clinical contraindications must be closely adhered to in the use of this drug

13 Because of the troublesome distention of the abdomen by gas, a combination of magnesium oxide 0 26 Gm (4 grains) (heavy) calcium and sodium bicarbonate 1 Gm (15 grains) of each may be given three times a day It is remarkable how this simple prescription often aids in the control of this condition Then too a prescription for tincture belladonna 8 cc (2 drams) with elixir phenobarbital 120 cc (4 ounces) in the dosage of one teaspoonful every three or four hours may be very helpful

14 Narcotics should not be given after the first day or two if they can be avoided They are apt to depress the patient make him vomit and have a harmful reaction It is better to give small doses of some soporific as phenobarbital medinal nembutal or bromides to control restlessness Frequently the patient is possessed with an almost ungovernable fear which is usually worse at night Most patients will not admit this fear of death but practically all of them have it Nurses and residents as well as the physician in charge should develop their knowledge of psychotherapeutics and control

many of the disturbances of these patients at night with psychic treatment rather than a hypodermic injection of a narcotic The patient feels better the next day if narcotics are restricted

15 The latest addition in the therapeutics of coronary occlusion is the use of anticoagulant therapy Recently a planned nation wide investigation of the value of *anticoagulants in coronary occlusion* was conducted by the American Heart Association The final report of this committee proves beyond a doubt that anticoagulants have *greatly decreased the incidence of embolic phenomena during the* course of coronary occlusion and has reduced its mortality Anticoagulants may be employed in the following way

a The prothrombin level is checked and if within the normal range the routine as described below is followed If below the normal range allowances must be made in determining the dicumarol dosage The desirable prothrombin level is 20 to 30 per cent of normal If it should drop below 20 per cent of normal hemorrhagic manifestations may develop It is always well to check or examine the urine for evidence of hemorrhage as the presence of hemorrhage from the kidney or from any other organ should cause one to think twice before giving the anticoagulant therapy

b To initiate therapy heparin which acts instantaneously *in doses of 100 mg intravenously every 4 hours for 36* hours is instituted at once The clotting time should be checked using Lee White s technique at least three times *during this period at intervals of approximately 8 hours* just before a succeeding dose is given This should serve as an index of the effectiveness of the heparinization and should warn of excessive dosage

c At the same time dicumarol is started giving 200 mg by mouth the first day and then 100 mg for every day thereafter that the prothrombin time is above *30* per cent of normal If the prothrombin time is between 20 and 30 per cent of normal 50 mg of dicumarol should be given The dosage should be omitted if the prothrombin level *should* fall below 20 per cent of normal It should be emphasized that this scheme is merely an outline of therapy and that the actual treatment should be adjusted to every individ

ual case One should correlate the patient s tolerance to the drug as shown by the daily prothrombin time with the dose administered in order to obtain the therapeutic level of 20 to 30 per cent of normal

d If the prothrombin level should drop below 20 per cent of normal close observation for hemorrhagic phenomena i e hematuria purpuric spots etc should be followed Prophylactic vitamin K in doses of 50 to 100 mg intravenously may be given if the level is below 15 per cent of normal If hemorrhagic phenomena should develop immediate transfusions must be given This therapeutic measure may be repeated according to the clinical response and the daily prothrombin estimations

Before leaving the subject of treatment I wish to emphasize that it is just as important to know what not to do in these cases as it is to know just what to do Therefore the following three medications must be avoided

1 Digitalis is usually contraindicated because it may irritate the heart and produce ventricular fibrillation or provoke a rupture of a necrotic area in the heart muscle If the patient is in congestive heart failure digitalis may be given

2 Nitrites must not be given to relieve pain as in angina pectoris They tend to promote vascular dilatation of the peripheral vessels which is already highly developed

3 Adrenalin is often used but it is a dangerous drug in these cases because of its tendency to cause ventricular fibrillation with sudden death

Acute Coronary Occlusion Thrombosis and Insufficiency
Summary of Treatment

1 Emergency treatment—1st to 14th day
  - *a* Permit patient to sit or lie in the position that is most comfortable for him
  - *b* Enforce absolute bed rest
  - *c* Apply external heat—blankets and hot water bottle
  - *d* Relieve pain by giving
    - (1) Papaverine hydrochloride 0 09 Gm (1½ grains)
    - (2) Atropine sulfate 0 45 mg (1/150 grain)

    } Intravenously immediately

many of the disturbances of these patients at night with psychic treatment rather than a hypodermic injection of a narcotic The patient feels better the next day if narcotics are restricted

15 The latest addition in the therapeutics of coronary occlusion is the use of anticoagulant therapy Recently a planned nation wide investigation of the *value of anticoagulants in coronary occlusion* was conducted by the American Heart Association The final report of this committee proves beyond a doubt that anticoagulants have *greatly decreased the incidence* of embolic phenomena during *the* course of coronary occlusion and has reduced its mortality. Anti coagulants may be employed in the following way

a The prothrombin level is checked and if within the normal range the routine as described below is followed If be low the normal range allowances must be made in determining the dicumarol dosage The desirable prothrombin level is 20 to 30 per cent of normal If it should drop below 20 per cent of normal hemorrhagic manifestations may develop It is always well to check or examine the urine for evidence of hemorrhage as the presence of hemorrhage from the kidney or from any other organ should cause one to think twice before giving the anticoagulant therapy

b To initiate therapy heparin which acts instantaneously *in doses of 100 mg intravenously every 4 hours for 36* hours is instituted at once The clotting time should be checked using Lee White s technique at least three times *during this period at intervals of approximately 8 hours* just before a succeeding dose is given This should serve as an index of the effectiveness of the heparinization and should warn of excessive dosage

c At the same time dicumarol is started giving 200 mg by mouth the first day and then 100 mg for every day there after that the prothrombin time is above *30* per cent of normal If the prothrombin time is between 20 and 30 per cent of normal 50 mg of dicumarol should be given The dosage should be omitted if the prothrombin level should fall below 20 per cent of normal It should be emphasized that this scheme is merely an outline of therapy and that the actual treatment should be adjusted to every individ

c Vasodilatation is obtained by the use of
(1) Nicotinic acid 50 mg (⅝ grain) t i d
(2) Copavin 60 mg (1 grain) t i d
d Digitalis is indicated only if heart failure is present
e Institute a light diet obesity diet is given when indicated
f Sedation
(1) Phenobarbital 46 mg (¾ grain) t i d
(2) Sodium bromide 1 Gm (15 grains) t i d
(3) Amytal 0 1 Gm (1½ grains) t i d
3 Convalescent treatment—two to six months
a Restrict activities markedly mild exercise only
b Avoid all types of physical mental or emotional strain
c Continue hospital drug therapy—xanthine derivative digitalis as previously indicated
d Keep up resistance and avoid infection
e Vitamins A B C and D should be administered especially during the winter months
f Restrict diet
g Give sedation as necessary

HEART FAILURE

For the purpose of convenience heart failure may be classified into left ventricular right ventricular and total or congestive heart failure Usually when the heart fails all chambers participate in the cardiac deficiency This however is not always true especially not in the earlier stages of failure when the symptoms of heart exhaustion may be predominantly either right chamber or left chamber variety But if heart failure particularly left sided persists the right side of the heart will eventually fail too Left ventricular failure is considered the commonest cause of right sided insufficiency Since incompetency of the left side of the heart occurs more commonly than that of the right it will be considered first and in more detail than the other kinds

Left Ventricular Failure

Etiology and Pathology The three outstanding causes of exhaustion of the left side of the heart are (1) persistent hypertension (2) aortic regurgitation and stenosis and (3) coronary disease In cases of long standing hypertension the heart usually bears up well under the strain of the high blood pressure and coronary narrowing with its subsequent malnourishment of heart muscles However

Followed by

(1) Papaverine hydrochloride 0 03 Gm (1/2 grain) (2) Atropine sulfate 0 45 mg (1/150 grain)	Subcutaneously intravenously or orally every four hours for 48 to 72 hours

If these do not relieve give pantopon 0 02 Gm (1/3 grain) hypodermically immediately (Morphine sulfate 16 to 30 mg (1/4 to 1/2 grain) may be administered but pantopon is preferable)

e Oxygen is given by nasal catheter tent or mask.

f Administer stimulants caffeine sodium benzoate 0 5 Gm (7 1/2 grains) subcutaneously or coramine 2 to 4 cc (1/2 to 1 dram) intravenously or intramuscularly if necessary

Avoid adrenalin and nitrites

If in profound shock apply tourniquet or bandage to arms and legs

Plasma in doses of 250 cc may be given slowly intravenously

g Employ anticoagulant therapy as follows

(1) Check prothrombin level so that it is 20 to 30 per cent of normal

(2) Administer heparin 100 mg intravenously every 4 hours for 36 hours Check clotting time at least three times during this period at 8 hour intervals just before a succeeding dose is given

(3) Start dicumarol at the same time giving 200 mg by mouth the first day and then 100 mg for every day thereafter that the prothrombin time is above 30 per cent of normal

(4) Give vitamin K 50 to 100 mg intravenously if the prothrombin level drops below 20 per cent of normal and hematuria purpuric spots or other evidences of hemorrhage develop If hemorrhages are severe also give a transfusion

h Give 50 to 100 cc. 50 per cent glucose with aminophylline 0 52 Gm (8 grains) intravenously immediately and twice a day as necessary

i Feed patient and assist with all movements

j Restrict visitors to immediate family

k Alkaline powders or citrocarbonate with tincture of belladonna are indicated for gaseous distention

l Enemas are contraindicated—give only mild cathartics as mineral oil 30 cc. (1 oz) daily

m Quinidine (if tolerated) 0 3 Gm (5 grains) t i d may be of value for frequent ectopic beats or arrhythmia

n Diet—when food can be taken it should be liquid or semisolid easily digestible and given in small quantities

o Codeine sulfate 30 to 60 mg (1/2 to 1 grain) or codeine phosphate 30 mg (1/2 grain) as necessary for cough

2 Intermediate treatment—2nd to 8th week

a Enforce complete bed rest for six to eight weeks

b Xanthine derivative is indicated (use one only)

(1) Aminophylline 0 19 Gm (3 grains) t i d

(2) Theobromine 0 3 Gm (5 grains) t i d

a gallop rhythm is heard on auscultation and progressive tachycardia may develop The patient begins to cough up frothy sputum sometimes tinged with small amounts of blood which is evidence of acute pulmonary edema

The patient may drown from edema of the lungs unless something is done immediately to relieve the left ventricular failure

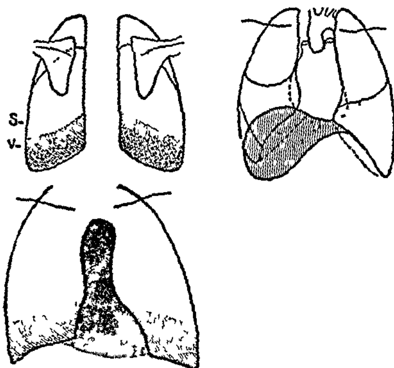


Fig 7 —Passive congestion At the bases of the lung area and decreasing from below upward are found relatively dark shadows which show little or no clearing on inspiration and which conceal in a varying measure the diaphragmatic costodiaphragmatic and lower cardiac outlines S— = diminished resonance V— = decreased fremitus

Examination of the patient at this stage reveals an individual in great discomfort He is usually half sitting up in bed gasping for air and harassed by cough and expectoration of the frothy sputum He is cyanotic covered with a cold clammy sweat and his pulse is so rapid that it is counted with difficulty

The symptoms of heart failure of the left ventricular type may be transitory lasting a few days or a week, or they may be persistent

added exercise an acute emotional strain loss of sleep or an acute upper respiratory infection in these cases will precipitate left ventricular failure

At the beginning hypertrophy of the heart is of the concentric type in which the left ventricular wall thickens at the expense of the chamber Dilatation then occurs in order to maintain cardiac output After a certain point active dilatation ceases to compensate and failure results As failure supervenes the left ventricle is no longer

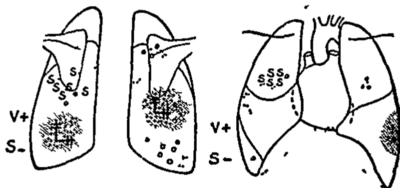


Fig 6—Passive congestion the result of cardiac weakness or failure in bronchopneumonia (edema of the bases of the lungs) V+ = increased fremitus S— = diminished resonance

capable of pumping all the blood it receives from the right ventricle Pulmonary vein hypertension engorgement of the lung vessels pulmonary congestion and pulmonary edema may follow serially

Signs and Symptoms In the early stage evidence of failure is strictly subjective The three prominent symptoms which indicate a diminution of the reserve force of the left heart are (*a*) dyspnea of the paroxysmal and usually nocturnal kinds (*b*) coughing especially in the morning caused by mild congestion in the lungs and (*c*) distressful sensation in the chest in the region of the sternum described by some as a tightness and by others as actual pain extending up into the neck and down into the arms Symptoms of these kinds nearly always develop in the presence of an enlarged left ventricle which usually precedes the onset of symptoms As the heart dilates a systolic mitral murmur develops but the murmur disappears as compensation returns If the lung congestion could be overcome promptly the acute attack would subside at other times the acute episode continues

tricuspid valve insufficiency and congenital heart lesions Constrictive pericarditis produces a syndrome possessing all the peripheral evidences of right ventricular failure without actual heart failure Emphysema and chronic bronchitis although they are at times associated with acute right ventricular failure are usually factors added to an already existing pulmonary disease which constitutes the main cause of the failure Cor pulmonale is the name applied to a syndrome characterized by dilatation hypertrophy and failure of the right ventricle caused by chronic pulmonary disease or pulmonary artery stenosis When an individual in the late teens 20 s, or early 30 s has failure the right sided type must be considered seriously just as left ventricular failure is the form that develops in people past 40 or 50 years of age

The sequence of events in right failure may be given briefly as follows Rheumatic infection in early life mitral disease indicated by mitral murmurs in subsequent years and the presence of a slight enlargement with the murmurs in the most active period of life but without evidence of failure In the early 30 s a combination of factors such as natural deterioration of the heart muscle enhanced by the handicap of a leaky valve plus some extra strain as a pregnancy in a woman contribute to an excessive burden on the heart especially of the right side This may be followed by an acute attack of right failure

Signs and Symptoms The features of acute right ventricular failure are also distinctive As the right ventricle begins to dilate and fail the venous pressure rapidly rises Ordinarily small rises in venous pressure are promptly reduced by the extra activity of the heart s action but in cases where the right chamber is involved the venous pressure rises higher and higher as indicated by enlargement and distention of the neck veins and enlargement and tenderness of the liver A symptom of right failure may be pain in the right upper quadrant of the abdomen brought on by exercise and relieved by rest It is often overlooked but can be an important clue It is explained as a manifestation of liver congestion and is comparable to the dyspnea on effort of early left failure Turgescence and cyanosis of the tissues about the upper extremities and marked cyanosis of the lips ascites and edema of the extremities develop later Sometimes on percussion and palpation the right auricle and ventricle are greatly dis

extending over a period of weeks or months There may be times when a remission of symptoms occurs alternating with acute crises of failure

Diagnosis The diagnosis of left ventricular failure is easily made The paroxysmal often nocturnal dyspnea congestion at the bases of the lungs and a sense of distress in the chest occurring in an individual who has hypertension aortic valvular disease or coronary insufficiency is usually all that is required for the diagnosis A usual clinical finding is the presence of an enlarged left ventricle An electrocardiogram which shows left axis deviation and at times inversion of the T wave in the standard leads of the electrocardiograph may aid in diagnosis

Prognosis when left ventricular failure sets in it is a general rule that complete recovery hardly ever occurs The reason for this is manifold The patient usually is in the advanced years of life when degenerative changes have already begun to take their toll the primary causes of left failure are conditions that are apt to be progressive in nature once they are established and finally for reasons not clearly understood when the mass of muscle of the left ventricle has its reserve force broken it is difficult or impossible to restore it to normal *However this is not the case in right ventricular* failure which is distinctly characterized by short periods of failure followed by long periods sometimes years of remission

It is evident then that when left ventricular failure becomes firmly established the outlook for the patient is distinctly bad and in the course of time the right chambers will be so strained that they too will fail The patient then has congestive heart failure or an admixture of left and right chamber deficiency The truest kind of left ventricular failure is seen in aortic stenosis and regurgitation In these cases there seems to be a pure forward failure of circulation without any evidence of back pressure in the lungs early in the disease

Right Ventricular Failure

Etiology and Pathology Heart failure essentially of the right ventricular kind occurs almost always in younger individuals under the age of 40 and is caused by lesions which throw the burden of the strain on the right chambers as mitral stenosis pulmonary fibrosis

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tended to the right of the sternum If they are not found on physical examination x rays frequently reveal their presence Pulsation of the large veins of the neck and liver may occur in right ventricular failure This usually develops when the tricuspid valve becomes incompetent due to dilatation or before dilatation comes on

Diagnosis The history of an attack of acute rheumatic fever and of an injured heart valve is important in diagnosis On examination the findings of a mitral valve disorder in conjunction with edema of the legs engorgement of the liver turgescence of the veins of the neck cyanosis and effusions into the peritoneal and pleural cavities are sufficient to make a diagnosis of right ventricular failure Further examination may reveal an enlargement of the right ventricle and an electrocardiogram may show right axis deviation and/or evidence of an abnormality of auricular fibrillation

Prognosis Right ventricular failure does not present as urgent a *case as that of the left ventricular type although the condition may* cause a great deal of distress The patient responds quite satisfactorily and may live on for many years suffering frequent bouts of acute right failure during this time

Congestive Heart Failure

Etiology and Pathology Congestive heart failure may be the result of left ventricular failure of right ventricular failure or of a combination of both The term congestive heart failure may be easily misinterpreted and because of its frequency of occurrence in any type of heart disease a brief description of it is given here

There is no unanimity concerning the mechanism of congestive heart failure and at the present time a great deal of discussion is carried on concerning the factors involved in this condition Many clinicians believe in the theory of either forward or backward failure most however believe that the two always occur together The forward failure theory embraces the idea that the output of the heart is diminished and therefore there is an anoxia in the tissues of the body especially in the brain As a result of this increase in capillary permeability edema and other clinical features of heart failure develop In the backward failure theory *it is supposed* that the weakened ventricle dilates and there is an accumulation of blood behind the dilated and weakened ventricle This then

results in increase of venous pressure increase of venous blood volume followed by increase of intercapillary pressure capillary anoxemia and finally edema and the resultant picture of congestive heart failure

Signs and Symptoms Of course the main feature of congestive heart failure is the inability of the heart to expel the amount of blood carried to it and the venous system as a consequence becomes over crowded with blood Decreased cardiac output prolongation of the circulation time increased venous pressure and dilatation of all chambers of the heart are characteristics of congestive failure

Differential Diagnosis Failure to mention the fact that the shock syndrome may *be confused at times with congestive heart failure may* be a serious omission The shock syndrome has some features in common with congestive heart failure especially the acute kind but there are differences which may be listed briefly as follows In the shock syndrome the trouble lies in the periphery and capillaries which are dilated and congested and not in the heart itself In shock the superficial veins especially those of the neck are empty while in failure they are gorged In shock the heart is very rapid and the pulse thready but the heart is not enlarged or otherwise diseased In heart failure of course the heart is usually enlarged and may be irregular and there may be valvular disturbances In shock the patient suffers from an oligemia while in congestive heart failure hydremic plethora is more apt to prevail Hemoconcentration is an outstanding evidence of shock but not of heart failure The treatment of congestive heart failure is usually pointed at relieving the peripheral vascular system of some of the excess blood while the *prime motive in the treatment of shock is to augment the blood* volume so that the heart will have enough blood to pump around the body Digitalis preparations are sheet anchors in the treatment of congestive heart failure but harmful consequences are the result of their administration to patients in shock

Prognosis The prognosis depends upon the underlying factors as the primary cause of the heart disease the degree of damage to the heart muscle and the response of the heart to treatment This last item is one that is difficult to evaluate at times but the age of the patient the size of the heart, and the faithfulness with which treatment is carried out all bear an influence in this regard

TREATMENT

Left Ventricular Failure The treatment of left ventricular failure to a large extent is built upon fundamental changes in the pathological physiology of the cardiovascular system The chief principles may be epitomized as follows

1 Absolute rest in bed for a number of weeks is imperative The patient obtains greater relief when allowed to sit up in bed than when lying flat

2 Oxygen is given especially if cyanosis or dyspnea persist it is wise to give it in any case of heart failure

3 Small doses of morphine 16 mg (1/4 grain) or pantopon 20 mg (1/3 grain) with atropine sulfate 0 9 to 0 45 mg (1/75 to 1/150 grain) hypodermically are sometimes necessary to quiet the patient and relieve dyspnea but morphine is a double edged sword in the therapeutics of heart failure and it must be used sparingly

4 Fifty to 100 cc of 50 per cent glucose solution with 0 5 Gm (7 1/2 grains) aminophylline may be given intravenously to augment the pulmonary circulation and relieve dyspnea

5 Digitalis purpura or digitalis lanata 0 09 Gm (1 1/2 grains) is usually indicated If one desires rapid digitalization strophanthin 0 65 mg (1/100 grain) may be given at once and repeated in six hours providing no digitalis has been given previously Ouabain five cat units may be given intravenously with six cat units of digitalis administered orally (see chapter on Heart Drugs)

6 Fluids should be encouraged (2 to 3 liters a day) orally However there is no apparent reason to force the fluids beyond the amount which the patient desires to take Sodium should be restricted to about 1 Gm (15 grains) a day To accomplish low levels of sodium in the diet salt free butter salt free bread and desalted milk should be used

7 Diuretics as diuretin are often too irritating to the stomach mercupurin in 1 or 2 cc doses or some like preparation may be given intravenously in the forenoon for a few days in succession Peripheral edema need not be present before mercupurin is indicated since the mercurial diuretics often relieve the dyspnea as well as the edema Anedemin the vegetable trochar of older physicians may be helpful

8 Cough is usually relieved when the circulation of the lungs is improved occasionally codeine phosphate or sulfate 30 mg (½ grain) may be given with ammonium chloride 1 Gm (15 grains) in a proper vehicle three or four times a day

9 When an acute attack of paroxysmal dyspnea sets in aminophylline 0 5 Gm (7½ grains) intravenously is generally sufficient to relieve the distress If not a narcotic as pantopon 20 mg (⅓ grain) may be resorted to Often the paroxysmal dyspnea that comes on at night may be prevented if the patient is given 0 19 Gm (3 grains) of aminophylline by mouth before going to sleep

10 The diet must be simple and non gas producing and the bowels controlled so distention of the abdomen with gas does not prevail as this augments the dyspnea already present from heart failure

11 If the veins of the neck are turgid and swollen when the patient is in a semireclining position and if he is cyanotic a venesection of 500 cc of blood is recommended Frequently this is followed by a prompt relief of the dyspnea

Right Ventricular Failure The fundamental principles emphasized in the treatment of left ventricular failure prevail also in right failure but there are a few important differences which I shall emphasize The rest oxygen aminophylline digitalis fluid limitation diuretics and diet may be patterned after the rules mentioned above The employment of diuretics has a special place in right ventricular failure because the symptoms are much more responsive to the mercurial diuretics than those of left failure Occasionally in right failure the venous congestion may be so great in the periphery and the venous pressure so high that nothing short of a venesection of one pint or more of blood will serve to relieve the patient This should be done immediately and repeated once or twice within a period of a week if necessary for the relief of symptoms In right ventricular failure an effusion of fluid is often present in the chest cavity compressing a lung this naturally is followed by an augmentation of the dyspnea Thus the heart failure which results in accumulation of fluid in the chest is in turn made worse by the ensuing reduction of lung volume and the vicious circle must be broken by the removal of the fluid by thoracentesis The same principle is applied to the accumulation of fluid in the abdominal sac

Congestive Heart Failure The treatment of congestive failure may be divided into (1) the immediate and (2) the remote The immediate treatment embraces the 11 items listed under the treatment of left failure The treatment of the so called remote factors is concerned with the precipitating cause of heart failure as infections indiscriminations and associated disorders Frequently in congestive failure as in right ventricular failure the cardiac insufficiency causes pleural effusion and the fluid must be removed to break the vicious circle caused by the effusion

ACUTE LEFT FAILURE SUMMARY OF TREATMENT

1 Absolute bed rest is enforced in semireclining position
2 Sedation (opiates) is indicated
 a Pantopon 20 mg (⅓ grain) | b Morphine 16 mg (¼ grain) | c Dilaudid 3 mg (1/20 grain) — Use one of these immediately and sparingly as needed for three or four days
 Follow with a barbiturate as
 a Phenobarbital 46 mg (¾ grain) t i d | b Nembutal, c Seconal — 0 19 Gm (3 grains) at night as needed — Tolerated best by the young and middle aged group
 Or with a bromide as
 a Triple bromide 1 Gm (15 grains) t i d | b Penta bromide 1 Gm (15 grains) t i d | c Sodium bromide 1 3 Gm (20 grains) t i d — Tolerated best by the older age group
3 Oxygen is given by nasal catheter tent or mask
4 Digitalization
 a Rapid methods
  (1) Cedilanid 1 6 mg intravenously followed by one tablet two or three times a day to maintain digitalization
  (2) Digilanid (digitalis lanata) 8 cc intravenously immediately then one tablet t i d until digitalized
  (3) Digifortis 3 cc intramuscularly or subcutaneously for two days follow with a maintenance dose of 1 cc daily
  (4) Ouabain 0 25 mg is administered intravenously and repeated in two hours
  (5) Strophanthin 0 006 Gm (1/100 grain) intravenously immediately (NOTE Do not use strophanthin or ouabain if patient was on digitalis!)
  (6) Digitoxin 1 2 mg for single dose digitalization The drug may be given orally or intravenously in the same dosage and results in digitalization within a few hours
  (7) Digoxin 1 mg intravenously for single dose digitalization may be used

b Slow methods

(1) Digitalis purpurea leaf 0 09 Gm (1½ grains) t i d until digitalized [approximately 21 mg per kg (1½ grains per 10 lb) body weight]

(2) Cedilanid 0 5 mg digoxin 0 25 mg or digitoxin 0 2 mg one tablet three times a day of any one of these preparations until digitalized

5 Administer 50 to 100 cc of 50 per cent glucose with 0 5 Gm (7½ grains) aminophylline intravenously immediately and b i d

6 Mercupurin 2 cc intravenously every other day for three times.

7 Cardiac diet is given

8 Xanthine derivative is indicated use one only

a Theobromine 0 3 Gm (5 grains) t i d

b Aminophylline 0 2 Gm (3 grains) t i d

c Theominal one tablet t i d

9 Papaverine hydrochloride 0 09 to 0 2 Gm (1½ to 2 grains)

10 Encourage fluids (2 to 3 liters a day) orally

11 Give patient reassurance (treat the psychic as well as the somatic disturbances)

Acute Right Failure

1 Enforce absolute bed rest in a semireclining position

2 Sedation is given as in Acute Left Failure

3 Digitalis is given as in Acute Left Failure

4 Oxygen is administered by nasal catheter tent or mask

5 Ammonium chloride 2 Gm (30 grains) t i d or
Ammonium nitrate 3 Gm (45 grains) t i d } For three days

6 Then give mercupurin 2 cc intravenously daily for three days

7 Encourage fluids (2 to 3 liters a day) orally

8 Remove pleural or ascitic fluid if patient is in distress

9 Venesection of 400 to 500 cc of blood may be necessary this must be done rapidly

10 Application of tourniquets to arms and legs

11 Magnesium sulfate 30 Gm (1 oz) daily three or four times

12 Cardiac diet consisting of soft low caloric and low salt foods is given

13 Xanthine derivative is indicated—theobromine or aminophylline as in Acute Left Failure

14 Codeine phosphate or sulfate are given for cough as in Acute Coronary Thrombosis

Chronic Myocardial Failure

1 Enforce absolute bed rest in a semireclining position

2 Digitalize the patient

3 Ammonium chloride 2 Gm (30 grains) t i d
Ammonium nitrate 3 Gm (45 grains) t i d } One or the other for three days

4 Then give mercupurin 2 cc intravenously every other day for three times

5 Administer 50 to 100 cc 50 per cent glucose with 0 5 Gm (7½ grains) aminophylline intravenously b i d

6 Sedation as in Acute Left Failure
7 Xanthine derivative as in Acute Left Failure
8 Magnesium sulfate 15 Gm (1/ oz) daily
9 Encourage fluids (2 to 3 liters a day) orally
10 Institute cardiac diet—soft low caloric low salt
11 High vitamin intake is important supplement diet at times with 10 000 units *vitamin B intramuscularly daily for one or two weeks*
12 Encourage movement of extremities
13 Check for *complications as infectious processes uremia thyrotoxicosis*

CHAPTER V

The Heart

(Continued)

THE ARRHYTHMIAS

Although disorders of cardiac rhythm are not always of grave significance they may cause the patient considerable distress Since the electrocardiograph has become more widely used in general practice many disorders of the heart beat have been described which were formerly diagnosed with difficulty if at all at the bedside However most irregularities can be diagnosed without the electrocardiograph

It is desirable to limit my discussion of the arrhythmias to those main types which are recognizable at the bedside These are

1 Sinus Arrhythmia
2 Premature Beats (extrasystoles ectopic beats)
3 Auricular Fibrillation
4 Auricular Flutter
5 Paroxysmal Tachycardia
6 Stokes Adams Syndrome

The significance of these irregularities of the heart beat depends upon the condition of the myocardium rather than on the disorder itself Although these arrhythmias do not always constitute emergencies it seems best to describe them so that their differential diagnosis at the bedside may be established

Sinus Arrhythmia

The simplest form of irregularity is sinus arrhythmia which frequently occurs in children and in the aged It is dependent upon a hyperirritability of the sinoauricular node or increased vagal tone

Etiology and Pathology The most common cause of sinus arrhythmia is myocardial disease or excessive dosage of digitalis in patients with a low tolerance for the drug At times obstruction of the blood supply to the sinoauricular node has been observed although generally the disorder has no significance and is associated with no pathological lesion

Signs and Symptoms Usually no symptoms are evidenced with this condition though occasionally there may be palpitation dizziness and even syncope if the rate is slow and continues over a period of time Nervous symptoms are common

Diagnosis The importance of sinus arrhythmia lies in the confusion it may cause with other kinds of irregularities In diagnosis one may note a variation in the period between the heart beats but there is no interference with transmission of the impulse that leaves the sinoauricular node It is recognized clinically by the fact that the heart beat becomes slower on expiration and more rapid on inspiration The relationship of this kind of irregularity to the act of respiration is usually sufficient to make the diagnosis of sinus irregularity or sinus arrhythmia

Prognosis While disturbances of sinus rhythm may at times be disagreeable they are rarely dangerous and are of little clinical importance

TREATMENT

In mild cases no special treatment is indicated and the best management consists in advising the patient to forget this disordered action of the heart beat

In more severe cases two things may be considered Omission of the toxic agent and administration of atropine sulfate 1/150 to 1/75 grain (0 4 to 0 8 mg) subcutaneously every 4 hours for marked bradycardia Occasionally 5 minims (0 3 cc) of adrenalin is used

Premature Beats (Extrasystoles Ectopic Beats)

Extrasystoles are premature heart beats caused by a premature contraction of the heart though the rhythm remains normal They originate independently of the impulses that come from the sinoauricular node These extra impulses coming from the auricle the ventricle or the a v node itself cause the premature contraction and consequently when the normal regular impulse from the sinus node passes down to the ventricle it finds the ventricle in the refractory period The diastolic period which follows the premature ventricular beat is therefore extraordinarily long This gives the patient a sensation of an unusually large heart beat and naturally causes him to become fearful or alarmed The beat due to the extrasystole then is

a small one and the next normal beat following it is a large one These big and little beats may be heard by listening over the heart but they may not be perceptible at the wrist

Etiology Although extrasystoles may occur at any age they are particularly common after the age of 50 The cause of this type of irregularity is unknown Functional disorders are apt to provoke these extrasystoles which disappear when the cause is removed Emotional strains excessive use of tobacco or alcoholic beverages and fever associated with infectious diseases have all been suggested as precipitating causes Extrasystoles may develop in individuals whose hearts are normal in every other respect or they may occur in association with serious cardiac diseases as mitral stenosis aortic regurgitation or coronary disease This is apt to cause considerable confusion in the proper interpretation of the irregularity While it is often said that premature beats are benign seldom serious and often disappear as promptly as they come leaving no heart disorder it must be kept in mind that the condition of the heart muscle rather than the presence of the irregularity itself is of first importance Therefore the extrasystoles especially those appearing after the age of 50 must be investigated thoroughly before the true significance is passed upon

Signs and Symptoms Very often individuals are unaware of the presence of premature heart beats then again they are felt as a dis agreeable sensation because of the pause after the normal beat If premature beats occur with great frequency dizziness and faintness may result In addition a sensation of shock and at times a tightness in the throat or chest may be felt

Diagnosis The differentiation between the auricular and the ventricular type of extrasystoles is usually made with certainty by the use of an electrocardiographic tracing Other times however the pa tient suffers from marked disturbance characterized by palpitation of the heart Patients with extrasystoles may or may not be incon venienced or alarmed by their presence however it must be empha sized that the extrasystole itself should not be regarded as a serious matter the gravity of the situation depends entirely upon whether cardiac disease occurs coincidentally with it Some believe that extrasystoles may cause the heart to be overworked and lead to heart failure but such an occurrence must be a rare outcome Although

Signs and Symptoms Usually no symptoms are evidenced with *this condition though occasionally there may be* palpitation dizziness and even syncope if the rate is slow and continues over a period of time Nervous symptoms are common

Diagnosis The importance of sinus arrhythmia lies in the confusion it may cause with other kinds of irregularities In diagnosis one may note a variation in the period between the heart beats but there is no interference with transmission of the impulse that leaves *the sinoauricular node It is recognized clinically* by the fact that the heart beat becomes slower on expiration and more rapid on inspiration The relationship of this kind of irregularity *to the act* of respiration is usually sufficient to make the diagnosis of sinus irregularity or sinus arrhythmia

Prognosis While disturbances of sinus rhythm may at times be disagreeable they are rarely dangerous and are of little clinical *importance*

TREATMENT

In mild cases no special treatment is indicated and the best management consists in advising the patient to forget this disordered action of the heart beat

In more severe cases two things may be considered Omission of the toxic agent and administration of atropine sulfate 1/150 to 1/75 grain (0 4 to 0 8 mg) subcutaneously every 4 hours for marked bradycardia Occasionally 5 minims (0 3 cc) of adrenalin *is used*

Premature Beats (Extrasystoles Ectopic Beats)

Extrasystoles are premature heart beats caused by a premature contraction of the heart though the rhythm remains normal They originate *independently of the impulses that come from the sino* auricular node These extra impulses coming from the auricle the ventricle or the a v node itself cause the premature contraction and consequently when the normal regular impulse from the sinus node passes down to the ventricle it finds the ventricle in the refractory period The diastolic period which follows the premature ventricular beat is therefore extraordinarily long This gives the patient a sensation of an *unusually* large heart beat and naturally causes him to become fearful or alarmed The beat due to the extrasystole then is

6 The difficulty may be relieved by avoidance of beverages containing caffeine of tobacco in excess and occasionally of alcohol

7 Digitalis usually makes the irregularity worse

The arrhythmia does not contraindicate exercise If an underlying myocardial disturbance is present however the treatment of the cardiac disease must be considered

Auricular Fibrillation

Auricular fibrillation is the commonest cardiac irregularity with the exception of premature contraction This disorder results from a disturbance in the mechanism of the heart impulse in which the wave contraction pursues a rapid and irregular continuous course around the auricles This leads to a fibrillary twitching without systematic regular contractions of the auricles The a v node is bombarded with impulses to which it fails to respond The effect on the ventricles results in an irregularity of the timing and strength of contractions of the ventricular chambers The ventricles beat at a rapid rate of 120 to 180 beats per minute Some of the contractions are too feeble to cause an opening of the aortic valve This leads to the phenomenon of pulse deficit in which the number of ventricular beats of the heart may be greater by 15 or 20 than the number of beats felt at the wrist

Etiology While many diseases of the heart provoke auricular fibrillation the main cause of this entity is unknown although many believe it is due to the establishment of a wave of excitation and contraction circulating irregularly about a variable ring of muscle in the auricles These in turn give off a stimuli to the ventricles which respond as rapidly as possible but with an irregular rate At times fibrillation exists without heart disease Histopathological examinations of fibrillating hearts fail to identify any specific tissue change Certain diseases however are known to be commonly associated with the onset of fibrillation They are rheumatic heart disease coronary disease hypertensive heart disease hyperthyroidism and sometimes syphilis White has summarized the analysis of McEachern and Baker of 575 cases of auricular fibrillation as follows Rheumatic heart disease 34 4 per cent coronary disease 31 1 per cent hypertension 16 9 *per cent thyrotoxicosis 7 5 per cent emphysema 5 0 per* cent syphilis 3 0 per cent and miscellaneous 2 1 per cent

it is thought by many that extrasystoles are to be ignored and that they mean nothing except a mild inconvenience of the heart rhythm I believe that they must be taken seriously and that a thorough investigation of the entire cardiovascular system is indicated However one must guard against passing a serious diagnosis when it is unwarranted because such an action may lead to cardiac neurosis When a physical cause for the condition cannot be found very often a psychological factor can be uncovered

Prognosis MacKenzie has pointed out that prognosis depends not on the presence or absence of premature beats but on the evidence of co existing organic heart disease and it is a well known fact that people with heart disease show a higher incidence and frequency of occurrence than do those with normal hearts

TREATMENT

In the treatment of extrasystole the following facts must be kept in mind

1 Quinidine in doses of 0 4 Gm (6 grains) orally every 2 hours until the arrhythmia is broken or until five doses have been given is effective The usual preliminary test dose of 0 2 Gm (3 grains) should be given first

2 Papaverine 60 to 90 mg (1 to 1½ grains) intravenously has been said to be as good as quinidine The prescribed dose may be repeated in ten minutes if necessary This drug is most effective in stopping ventricular premature systoles which may forestall fatal ventricular fibrillation

Papaverine also is followed by good results when given orally 0 2 Gm (3 grains) four or five times daily This drug is particularly good in cases with coronary insufficiency as it is a mild sedative and good coronary dilator

3 Potassium acetate 3 Gm (45 grains) upon retiring and repeated after 3 hours if the first has not been effective has been used with beneficial results

4 Aminophylline 0 2 Gm (3 grains) three or four times daily may prove effective

5 Small doses of bromides 0 3 Gm (5 grains) three times a day or phenobarbital 30 mg (½ grain) two or three times a day are used to sedate an overirritable and nervous patient

TREATMENT

1 The patient must be confined to bed during the early stages of fibrillation A vigorous attempt must be made to control this irregularity as soon as possible in order to forestall such complications as heart failure death from ventricular fibrillation and the formation of emboli

2 The type and degree of cardiac damage must be determined at once This is important because it is obvious that if the cause of the disorder is hyperthyroidism the treatment will be quite different than if the cause is mitral stenosis or rheumatic heart disease

3 There are two drugs for auricular fibrillation—quinidine sulfate and digitalis

Quinidine sulfate is a satisfactory drug in the following cases

1 Young individuals who have no heart failure
2 Where the irregularity has been of short duration
3 Patients without advanced valvular damage

a Quinidine sulfate should be given in small doses at first and then increased gradually to 0 4 Gm (6 grains) every 2 hours

b Quinidine may be given intramuscularly if more rapid action is required A prescription which is easily prepared and stored and which contains 0 15 Gm (2¼ grains) quinidine to the cc may be made as follows

Quinidine hydrochloride	1 Gm	(15 grains)
Antipyrine	1 Gm	(15 grains)
Urea	1 5 Gm	(20 grains)
Water (distilled) to make	100 cc	(3⅓ oz)

This should be sterilized in a Berkefeld filter It can then be stored in ampules or stoppered bottles This preparation is advocated for intramuscular use in cases where there is delayed absorption from the gastrointestinal tract and when rapidity of action is necessary It may be used whenever oral administration of quinidine is indicated The dosage is 0 45 to 0 6 Gm (6 75 to 9 grains) In from one and one half to two hours the dose may be repeated If no favorable response is elicited the dose may be increased

c Quinidine may be used intravenously but is rarely employed because of the danger associated with it For intravenous administration 4 Gm of quinidine dissolved in 500 cc of 5 per cent glucose is given by very slow intravenous drip

d Strychnine sulfate 1/60 grain (1 mg) three times daily has been used in combination with quinidine to facilitate its action

Signs and Symptoms Auricular fibrillation may begin abruptly and lead to cardiac failure if the heart muscle is badly damaged Subjectively there is usually a sense of palpitation associated with shortness of wind faintness and exhaustion Pain is seldom present unless the fibrillation is a part of coronary disease The discomfort caused by the onset of fibrillation usually causes the patient great mental agony

Auricular fibrillation may be one of two types from the clinical standpoint (*a*) Paroxysmal or intermittent and (*b*) continuous or permanent The paroxysmal type may last a short time only and cause little or no disturbance of the cardiac function while the permanent type is bound to cause embarrassment of the heart The intermittent acute paroxysmal fibrillation usually develops in normal hearts frequently it is precipitated by excessive drinking or heavy smoking A day of rest in bed usually is sufficient to restore the cardiac rhythm to normal If the heart is not enlarged and if no valvular disease coronary occlusion or evidences of failure are present quinidine in doses of 0 3 to 0 6 Gm (5 to 10 grains) every four hours restores the regular rhythm within a few days Permanent or continuous auricular fibrillation usually develops in individuals who have an established cardiac defect but if it develops in an older person past 50 years of age and the immediate cause is not perfectly clear the possibility of a hidden hyperthyroidism should be kept in mind

Diagnosis The diagnosis of auricular fibrillation can usually be made by physical examination The irregular beating of the heart and the presence of pulse deficit are enough to confirm the diagnosis Occasionally premature contractions may simulate auricular fibrillation If possible one should always have an electrocardiographic tracing done in order to be certain of the diagnosis

Prognosis The prognosis of continuous fibrillation is much more unfavorable than the intermittent form for the presence of the fibrillation causes the heart reserve to become depleted However the arrhythmia in some cases may be present for many months or even years without causing cardiac failure In children prognosis is poor because it is usually associated with severe myocardial lesions and heart failure

but it is known that the mechanism is due to the development of a circus rhythm in the auricles with a resulting varying degree of auriculoventricular block

Signs and Symptoms The attack of flutter causes the individual to feel a marked palpitation of the heart dizziness giddiness and sometimes fainting and exhaustion occur In addition the pulse is very rapid

Diagnosis A clinical diagnosis of auricular flutter is based on the sudden onset of attacks of rapid pulse and the duration of the attack This disorder is often confused with paroxysmal tachycardia and an electrocardiographic tracing may be necessary for the differentiation

Prognosis An attack of auricular flutter may be short in duration lasting for one half hour or it may continue for days weeks or even months The outcome of auricular flutter depends on the condition of the heart muscle itself The most important phase of our knowledge of flutter consists in our ability to convert the flutter into fibrillation and the fibrillation to normal rhythm

TREATMENT

The treatment of auricular flutter is as follows

1 Digitalis is the drug of choice and digitalization of the patient corrects the flutter to fibrillation When the fibrillation replaces the flutter the withdrawal of the digitalis results in the return of the heart rhythm to normal The rapid or slow methods of digitalization may be used as outlined on pages 94 and 95

2 Usually quinidine is less effective in flutter than in fibrillation but it is indicated when attacks are paroxysmal and when congestive failure heart damage and emboli are not part of the picture During this kind of therapy the patient must be closely watched as the doses are large and toxicity may follow A test dose of 0 2 Gm (3 grains) should be given Then if no unfavorable reaction occurs 0 4 Gm (6 grains) may be given orally and repeated every four hours for six or seven doses If good results do not follow the dosage may be increased but the patient must be carefully watched all the time When rhythm returns to normal the dose is reduced to 0 2 to 0 4 Gm (3 to 6 grains) t i d and continued for several weeks at least This drug is best not given intravenously Some say that if given with strychnine 1 5 to 2 mg (1/10 to 1/30 grain) t i d quinidine therapy is more

Quinidine is contraindicated for patients with long standing heart failure or advanced valvular disease and for older people

When fibrillation accompanies heart disease especially congestive failure mitral stenosis or chronic arteriosclerosis digitalis in full dosage *is the preferred drug At times auricular fibrillation with severe* myocardial failure may threaten life and emergency treatment must be instituted

a Strophanthin 0 65 mg (1/100 grain) may be given intravenously and repeated every 12 hours for three or four doses It must be emphasized that strophanthin is contraindicated if the patient has been digitalized within a week of the time of giving strophanthin

b Lanatoside C (cedilanid) 1 6 mg in single or divided doses may be given

c Digitoxin 1 26 mg (three cat units) may be given for single dose digitalization either orally or intravenously

d Ouabain 0 5 mg (five cat units) intravenously reduces the ventricular rate and is beneficial in treating arrhythmias of auricular origin One hour after the first dose of ouabain four to eight cat units of digitalis leaf should be given orally Twenty four hours after the initial dose digitalis is given in maintenance doses of 1 grain or 0 06 Gm (one cat unit) daily Ouabain should not be used when digitalis has been used in the preceding week

e Sometimes auricular fibrillation and cardiac embarrassment may require oxygen or the intravenous injection of 50 cc to 100 cc of 50 per cent glucose solution with the addition of 0 5 Gm (7½ grains) aminophylline to reduce pulmonary congestion promote diuresis and allay the dyspnea brought on by lung congestion

4 Potassium acetate 2 Gm (30 grains) four times daily has been reported to control the arrhythmia as has quinacrine (atabrine) 0 4 Gm (6 grains) intramuscularly

Auricular Flutter

Auricular flutter is a disorder characterized by a regular but very rapid rate of auricular contraction with regular ventricular contractions at about one half the auricular rate The rate of the auricular beat may be between 200 and 400 per minute the ventricular beat may be from 100 to 200 per minute

Etiology Like auricular fibrillation auricular flutter is a common occurrence in patients with heart disease The cause is obscure

ganic disease as coronary occlusion The exact differentiation requires an electrocardiogram

Prognosis In general prognosis is good and it is only when attacks are very long or recurrent that it is guarded

TREATMENT

There is no sovereign method of treatment for an attack of paroxysmal tachycardia

1 The patient should be allowed to rest in the position which he finds most comfortable This is usually lying supported by pillows but some prefer to stand or sit

2 Food should be chosen carefully for its high nutritive value and its capability of being taken easily It should be given in small quantities

3 Ice bags may be used to relieve local pain iced drinks may be given Occasionally ice over the precordium is all that is necessary to relieve an attack

4 Morphine may be needed to relieve the dyspnea and if acute pulmonary edema is present oxygen is necessary

5 Sometimes digitalis controls paroxysmal tachycardia while at other times quinidine is more effective Some believe that digitalis may bring on an attack and should be avoided

6 Frequently ocular pressure breath holding or pressure on the carotid artery below the angle of the jaw will stop this arrhythmia It should be emphasized that this pressure on the carotid must be exerted on the carotid sheath for periods of 5 10 or 15 minutes Most people attempting compression for the control of the paroxysm exert the pressure for too short a period of time to obtain relief Syrup of ipecac 1 to 2 drachms (4 to 16 cc) may prove helpful in stimulating the vagus

7 When treatment such as carotid or ocular pressure and breath holding is unsuccessful magnesium sulfate may be given intravenously in doses of from 10 to 20 cc of 10 to 20 per cent solution The stronger doses are apt to be more successful This form of therapy is not associated with any serious toxic reactions though transient disturbances of conduction and ventricular extrasystoles may occur

8 Mecholyl subcutaneously may be given The initial dose is 20 mg (⅓ grain) If necessary this dosage may be repeated in 20

effective and smaller doses are necessary Sometimes digitalis and *quinidine in combination may prevent or abort attack*

3 Recurrent attacks of flutter have been observed They may be controlled by the use of digitalis or strophanthin or the other drugs as indicated above *The regulation of the flutter has a favorable effect upon the accompanying signs and symptoms of heart failure* Edema disappears dyspnea clears away and palpitation ceases

Paroxysmal Tachycardia

Paroxysmal tachycardia is an arrhythmia characterized by the abrupt onset of an extremely rapid beating heart The condition is most often associated with hyperthyroidism especially during the *first few days following an operation of the thyroid gland As can* be expected distressing symptoms are especially prevalent in individuals having serious organic heart disease

Etiology *Paroxysmal tachycardia is caused by ectopic beats rising* from a single focus in the heart muscle There is no specific pathological change known to account for it It may be associated with coronary disease or rheumatic heart disease but it often develops independent of any organic disorder and is known to occur with fatigue anxiety states or digestive disturbances

Signs and Symptoms The episode of tachycardia begins abruptly and may last for a few minutes or a month and it may end as quickly as it started During the attack the patient suffers from a sense of extreme exhaustion dyspnea irritability and sometimes syncope Pulsations of the vessels of the neck may be violent The attack may result in peripheral vascular collapse

Differential Diagnosis A differentiation must be made between auricular flutter paroxysmal auricular fibrillation and paroxysmal tachycardia In paroxysmal tachycardia there is less likely to be an organic disease in the background while in flutter and fibrillation organic disease is the common rule *Patients with paroxysmal tachycardia* are usually young people who are emotionally unstable A distinction is often made between auricular ventricular, and nodal paroxysmal tachycardia *In the auricular form the attack is usually* minor and is controlled by stimulation of the vagus nerve Ventricular paroxysmal tachycardia is similar but may be associated with or

ganic disease as coronary occlusion The exact differentiation requires an electrocardiogram

Prognosis In general prognosis is good and it is only when attacks are very long or recurrent that it is guarded

TREATMENT

There is no sovereign method of treatment for an attack of paroxysmal tachycardia

1 The patient should be allowed to rest in the position which he finds most comfortable This is usually lying supported by pillows but some prefer to stand or sit

2 Food should be chosen carefully for its high nutritive value and its capability of being taken easily It should be given in small quantities

3 Ice bags may be used to relieve local pain iced drinks may be given Occasionally ice over the precordium is all that is necessary to relieve an attack

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Signs and Symptoms *The episode of tachycardia begins abruptly* and may last for a few minutes or a month and it may end as quickly as it started During the attack the patient suffers from a sense of ex treme exhaustion dyspnea irritability and sometimes syncope Pul sations of the vessels of the neck may be violent The attack may result *in peripheral vascular collapse*

Differential Diagnosis A differentiation must be made between auricular flutter paroxysmal auricular fibrillation and paroxysmal tachycardia In paroxysmal tachycardia there is less likely to be an organic disease in the background while in flutter and fibrillation organic disease is *the common rule Patients with paroxysmal tachy* cardia are usually young people who are emotionally unstable A distinction is often made between auricular ventricular and nodal paroxysmal tachycardia In the auricular form the attack is usually minor and is controlled by stimulation of the vagus nerve Ventricu lar paroxysmal *tachycardia is similar but may be associated* with or

ally patients recover from such a seizure though occasionally it is fatal If the seizure lasts more than 2 minutes the patient usually dies

Diagnosis Complete heart block is readily recognized in most cases because the heart rate is so slow and regular and the pulse rate drops to 30 or 40 beats a minute The patient is usually comfortable unless evidences of heart muscle exhaustion set in

There is usually some degree of chronic heart block and an electrocardiogram reveals complete dissociation of the auricular and ventricular activity

Prognosis Some patients with the Stokes Adams syndrome live for 10 to 25 years after the initial episode while others die in the first attack I have observed a patient with complete heart block and a rate that ranged from 20 to 35 beats per minute for a period of 25 years

TREATMENT

The patient with Stokes Adams disease or chronic bradycardia may have his life prolonged by many years with successful treatment The ultimate outcome depends not on the seizures but on the condition of the heart muscle and the lesion producing the bradycardia

1 During the attack 1 cc of epinephrine 1 1000 solution is given subcutaneously at once and repeated every two hours for several doses

2 Ephedrine sulfate 16 to 32 mg (¼ to ½ grain) in capsules may be administered by mouth every three or four hours

3 Barium chloride 32 to 64 mg (½ to 1 grain) three or four times a day has also been recommended

4 After the acute episode is over the most effective treatment consists of giving thyroid extract 64 mg (1 grain) two or three times a day

5 Atropine sulfate 0 8 mg (1/75 grain) twice a day or tincture of belladonna 1 cc two or three times a day may be used until evidence of atropinism such as dryness of the mouth or visual disturbances occurs

6 Benzedrine 5 to 10 mg three to four times a day may be used

7 Metrazol 15 mg two or three times a day may be given

minutes or half an hour Before this drug is employed, a syringe containing 0 6 mg ($\frac{1}{100}$ grain) atropine sulfate should be ready to counteract any untoward reactions Mecholyl should not be used in those with bronchial asthma or coronary artery disease Acetyl β methylcholine 20 mg may also be given

9 Increased injections of neosynephrine starting at 0 15 mg to 0 80 mg has been seen to increase the blood pressure with a simultaneous reversion to normal rhythm

Occasionally all these measures fail and the attack ceases as spontaneously as it began In most difficult cases of paroxysmal tachycardia it is important to remember that administration of any of the above remedies may fail to control the episode but they should be repeated again and again and finally the paroxysm may be eliminated

Heart Block

White defines heart block as the result of depression of the specialized tissues that normally initiate the heart beat and conduct it to the muscle of both ventricles In itself heart block does not cause the patient s death though patients may be inconvenienced by a more severe grade of block developing where it has existed for some time Heart failure usually terminates the life of the patient

Etiology and Pathology This disorder most often occurs in individuals past 50 years of age and is commonly associated with diseases of the coronary arteries usually arteriosclerotic occlusion of some of the branches or rheumatic fever Occasionally the lesion is syphilitic in nature and involves the myocardium

Signs and Symptoms The Stokes Adams syndrome is distinguished by paroxysmal attacks of bradycardia associated with fainting dizziness and sometimes epileptiform convulsions The paroxysms occur irregularly coming on every few days for a period of several months and then disappearing for a period of months or years Sometimes the condition changes to normal rhythm and then back again to complete block within a period of 5 minutes

The onset is abrupt and without apparent cause an attack frequently develops while the patient is at work or occasionally while he is at rest in bed The seizure is characterized by sudden dizziness and giddiness followed by loss of consciousness There is a tonic followed by a clonic convulsion accompanied by foaming at the mouth Usu

no signs of the endocardial lesion However a mitral systolic murmur appearing during the course of rheumatic fever and persisting after the acute phase would lead one to believe that the murmur was of endocarditic origin

Diagnosis A history of rheumatic fever is of value in diagnosis However the diagnostic identification mark is the presence of a soft blowing murmur over the valve area As the mitral valve is most commonly involved a soft systolic mitral murmur is usually present Unless one has examined the heart carefully every day of the sickness the presence of a murmur may lose its significance It may be a new development or it may have been there before the onset of the present illness A murmur alone must not be taken as positive evidence of endocarditis because in any acute febrile disease a systolic murmur may result from the slight cardiac dilatation which develops

Prognosis Sometimes the lesion of acute endocarditis heals in about 1½ months although prolonged bed rest is advisable Patients with even the simplest form of acute endocarditis will not recover but will develop complications unless rest in bed is enforced

TREATMENT

In the treatment of simple endocarditis it is not the dramatic exhibition of any one specific measure but the judicious use of many different measures that brings about the cure of the patient

1 Absolute rest in bed is necessary Sometimes the lesion heals in about one and one half months but prolonged rest is advisable A question often asked is When should a patient with simple endocarditis be allowed out of bed? Freedom from fever for a period of one month a drop of the leukocytes to normal a normal sedimentation rate and a normal red cell count with a heart rate under 90 per minute are evidences that the heart lesion has healed completely or almost completely I have found the sedimentation rate to be of distinct value in determining when the patient should be allowed more freedom Usually the fever pulse rate and leukocyte count return to normal long before the sedimentation rate does and therefore this test is of particular value

2 The medical treatment is of less importance than the general measures Nevertheless certain drugs appear to have a favorable action in these cases

CHAPTER VI

The Heart

(Continued)

ENDOCARDITIS

Acute Endocarditis

Acute endocarditis may be classified into simple or benign and the ulcerative sometimes called malignant and subacute bacterial endocarditis The benign or verrucose type is by far the commonest of the three It is practically always the result of acute rheumatic fever or tonsillitis and is considered to be caused by a mild form of streptococcus Rheumatic endocarditis is the name usually applied to the benign condition The malignant form is caused by suppurative organisms as staphylococci pneumococci streptococci and gonococci The engraftment of Streptococcus viridans on a valve already damaged by rheumatic infection is called subacute bacterial endocarditis

Acute } 1 Rheumatic (benign)
2 Bacterial (malignant)
3 Subacute bacterial endocarditis (Endocarditis lenta)

Pathology The changes in the heart valves in the simple form are characterized by small beadlike nodules in the subendocardial tissue near the edge of the valve Later deposits of fibrin and connective tissue result in the warty or verrucose type of vegetation While all cases of the simple form of endocarditis do not heal most of them do As healing occurs scar tissue in the valve leaflets contracts and insufficiency of the valve develops The degree of functional impairment occurring in a valve depends of course on the severity of the acute endocardial lesion In those cases in which the *inflammatory lesion in the valve fails to heal in the usual period* of a few months an accompanying acute myocarditis and likely pericarditis are present When healing occurs the patient remains well for many years until the remote consequences of the defective valve action cause embarrassment of the heart muscle with beginning failure 20 to 25 years later

Signs and Symptoms In the early stages of the disease there are

no signs of the endocardial lesion However a mitral systolic murmur appearing during the course of rheumatic fever and persisting after the acute phase would lead one to believe that the murmur was of endocarditic origin

Diagnosis A history of rheumatic fever is of value in diagnosis However the diagnostic identification mark is the presence of a soft blowing murmur over the valve area As the mitral valve is most commonly involved a soft systolic mitral murmur is usually present Unless one has examined the heart carefully every day of the sickness the presence of a murmur may lose its significance It may be a new development or it may have been there before the onset of the present illness A murmur alone must not be taken as positive evidence of endocarditis because in any acute febrile disease a systolic murmur may result from the slight cardiac dilatation which develops

Prognosis Sometimes the lesion of acute endocarditis heals in about 1½ months although prolonged bed rest is advisable Patients with even the simplest form of acute endocarditis will not recover but will develop complications unless rest in bed is enforced

TREATMENT

In the treatment of simple endocarditis it is not the dramatic exhibition of any one specific measure but the judicious use of many different measures that brings about the cure of the patient

1 Absolute rest in bed is necessary Sometimes the lesion heals in about one and one half months but prolonged rest is advisable A question often asked is When should a patient with simple endocarditis be allowed out of bed? Freedom from fever for a period of one month a drop of the leukocytes to normal a normal sedimentation rate and a normal red cell count with a heart rate under 90 per minute are evidences that the heart lesion has healed completely or almost completely I have found the sedimentation rate to be of distinct value in determining when the patient should be allowed more freedom Usually the fever pulse rate and leukocyte count return to normal long before the sedimentation rate does and therefore this test is of particular value

2 The medical treatment is of less importance than the general measures Nevertheless certain drugs appear to have a favorable action in these cases

a Sodium salicylate 1 Gm (15 grains) with sodium bicarbonate 0 6 Gm (10 grains) may be given every three hours with plenty of water until the patient objects to the untoward reactions of the salicylates as ringing in the ears and excessive sweating At times if tolerated patients may need larger doses If not tolerated orally we have found 5 Gm (75 grains) of sodium salicylate given as a starch retention enema two or three times a day to be of great value Salicylates may be given *via* the parenteral route but there is no particular advantage in administering them this way If they are not tolerated one may have to resort to the use of amidopyrine 0 6 Gm (10 grains) four times a day in order to relieve the patient of pain If this drug is used one must watch the white count closely

b If heart failure should supervene this condition must be treated with digitalis diuretics and low sodium diets

c Most patients with acute endocarditis suffer from hypochromic normocytic anemia This is overcome by administration of citrate iron as iron ammonium citrate 2 Gm (30 grains) three times a day

d Since these patients are usually indisposed for a number of weeks or months with fever and other toxic manifestations of the disease the appetite may be very poor and a vitamin deficiency may result It is wise to supplement the diet with a number of the essential vitamins which have been standardized therapeutically as concentrated cap sules of cod liver oil and vitamins B and C

Acute Ulcerative (Bacterial) Endocarditis

Acute bacterial endocarditis is usually caused by hemolytic streptococcus staphylococcus gonococcus or pneumococcus Rarely some other organism is responsible Acute bacterial endocarditis like pericarditis is seldom a primary disease and is usually the result of an infection elsewhere in the body as pneumonia gonorrhea or general sepsis

The lesion on the valve differs from that of the simple endocarditis probably more in degree than in kind There is a rapidly growing cauliflowerlike vegetation which develops from the presence of the organism in the blood stream While the appearance of the vegetation may differ depending on the type of organism producing it the nature of the lesion is practically the same with all organisms

Signs and Symptoms The onset of this disease is commonly abrupt but the endocarditis is usually completely overshadowed by the severity of the constitutional symptoms of the original disease The diagnosis of heart involvement therefore may be delayed for

some time The rapidity of the progress of acute ulcerative bacterial endocarditis has given rise to the term malignant for these cases

Some of the clinical features found are sepsis high fever usually leukocytosis prostration and sometimes delirium or coma

It has been customary to split this kind of endocarditis into the cardiac the typhoid and the so called septic types but these terms have reference only to the organs which bear the brunt of the infection For example if the symptoms are predominantly referable to the heart it is said the patient has the cardiac type if the symptoms are those of long-continued sepsis it is called the septic type while the typhoid class refers to those patients with bowel involvement The fever tachycardia pallor prostration and murmurs of the heart are the chief signs The spleen may be considerably enlarged though this may not develop until later in the course of the disease Despite the extensive involvement of the heart valves at autopsy the physical signs as valvular murmurs are often not very pronounced Usually the mitral valve is involved although right sided endocarditis may occur also

Many times the evidences of endocarditis of this type are found outside the heart itself For example an embolic particle may break off the cauliflowerlike vegetation and be carried into the brain causing hemiplegia and secondary abscess or it may pass on into the large vessels leading to the extremities resulting in embolic occlusion of the main artery and gangrene

Diagnosis Diagnosis of the condition is confirmed by a positive blood culture and the findings of a loud changing cardiac murmur

Prognosis Patients with acute bacterial endocarditis have a very grave prognosis However with the development of the sulfonamides and antibiotics the outlook for these patients may be entirely changed

TREATMENT

1 Penicillin from 300 000 to 1 000 000 or 2 000 000 units every 24 hours may cure the patient if treatment is initiated early It is given either intravenously or intramuscularly in combination with the sulfonamides or alone

2 Sulfadiazine has been shown to be of definite value at times resulting in cures and at other times relieving the patient of drenching sweats prolonged fever and associated debilitation Further refer

ence to the use of this drug will be made under Subacute Bacterial Endocarditis

Vaccines therapeutic sera and administration of dyes as gentian violet and mercurochrome have failed to alter the downward trend of endocarditis

Subacute Bacterial Endocarditis

Any patient with valvular heart disease caused by rheumatic fever is a candidate for one of four complications (1) Failure of the heart (2) auricular fibrillation (with failure or embolic phenomena) (3) embolism or (4) subacute bacterial endocarditis Subacute bacterial endocarditis is not as acute as the so called malignant form since it runs a slower course lasting over a period of several months or even a few years Nevertheless it is as likely to cause the patient's death as the short and stormy acute (malignant) bacterial endocarditis Although subacute bacterial endocarditis is not a common disease it is important because it may be simulated by so many other disorders and because of the almost universally fatal prognosis and inadequacy of treatment before the advent of the sulfonamide drugs A diagnosis of subacute bacterial endocarditis erroneously made or failure to recognize its presence is unfortunate for both patient and physician

Etiology and Pathology The chief cause of subacute bacterial endocarditis is a streptococcus usually of hemolytic or viridans variety less often the pneumococcus Bacillus influenzae or staphylococcus is involved This type of endocarditis occurs most frequently in patients who are between the ages of 15 and 30 years having valvular lesions or certain congenital abnormalities About two thirds of *the patients seen are males*

The chief cardiac lesion is valvular consisting of a new granulomatous cauliflowerlike vegetative growth larger than rheumatic vegetations that are engrafted on the valve One of the chief characteristics of this vegetation is its tendency to spread to the mural endocardium

Signs and Symptoms The five main characteristics are (1) pallor (2) fever (3) asthenia (4) presence of an old valve lesion or of a congenital lesion and (5) an enlarged spleen Other prominent features are weight loss anemia slight leukocytosis (occasional leu

kopenia) with increased stab forms elevated sedimentation rate heart murmur red blood cells in the urine petechial hemorrhages Osler s nodes clubbed fingers and a positive blood culture

Practically all the systems of the body may be involved at one time or another during the course of subacute bacterial endocarditis

1 Nervous system Symptoms are due to systemic infection or toxemia Emboli to the brain may result in hemiplegia convulsions coma or retinal hemorrhages (Roth s sign)

2 Cardiorespiratory system Symptoms of heart failure are not common Murmurs of an old heart lesion may be changed by the development of vegetations Vegetations or bacteria may break off enter the blood stream and produce pulmonary infarction

3 Gastrointestinal system Anorexia vomiting and diarrhea which may be bloody due to showers of emboli often occur

4 Genitourinary system Focal embolic glomerulonephritis or renal infarction with red blood cells white blood cells and albumin in the urine are almost always present

5 Cutaneous manifestations and extremities Crops of petechiae in the mucous membranes and skin splinter hemorrhages under the fingernails Osler s nodes clubbed fingers and gangrene of an ex tremity from embolism in a peripheral vessel may develop

6 Hematopoietic system Secondary anemia and leukocytosis (often 12 000 to 18 000) with shift to the left in the Schilling count are common The sedimentation rate is increased Histiocytes may be present

The onset of the disease is characteristically insidious and in the first stages the symptoms are those of a low grade infection The most frequent early complaints are weakness fever cardiac symptoms and arthralgia or if the onset is sudden chills sweats and emboli may be foremost In the later phases of the illness embolic manifesta tions are prominent The course is typical It may be stormy and end fatally in a few months but usually it is characterized by remis sions representing semihealing of the heart valve lesions during which the patient may be afebrile for months Pallor remains exacerbations occur and death comes within a year or two I have seen patients recover though they have presented the typical picture of subacute bacterial endocarditis except for the positive blood culture

Diagnosis The diagnosis is proved by the presence of a positive blood culture The simple forms of endocarditis may recur from time to time and closely simulate subacute bacterial endocarditis but patients with the latter disease usually die, while those with simple endocarditis nearly always live The differentiation here is of more than just academic interest With few exceptions I demand a positive blood culture before labeling a patient with a diagnosis of subacute bacterial endocarditis

This disease is frequently confused with neurasthenia typhoid fever, undulant fever tularemia recurrent rheumatic endocarditis or pyemia without endocarditis Malignancy, blood dyscrasias as purpura hemorrhagica leukemia and pernicious anemia Banti s disease, and myxedema must also be considered Cases of sudden onset may be confused with influenza and malaria

Prognosis Subacute bacterial endocarditis is not as acute as the so called malignant form since it runs a slower course lasting over a period of several months or even a few years Nevertheless it is as likely to cause the patient s death as the short and stormy acute (malignant) bacterial endocarditis Even with the use of antibiotics in satisfactory doses prognosis is not as good as is often thought since there is still a mortality rate of approximately 30 per cent in this disease

TREATMENT

The treatment of subacute bacterial endocarditis is dependent upon a number of factors the most important being the organism involved Either penicillin streptomycin or sulfadiazine may be used depending upon to which one of these drugs the organism is most sensitive

1 Penicillin is most commonly employed in the intermittent intramuscular form injections being given every 2 to 3 hours The total daily dose depends primarily upon the patient s clinical response organism sensitivity as determined in vitro is not always a reliable guide *By and large authorities are agreed that the average* case requires approximately 500 000 units of penicillin daily although more persistent cases of course will necessitate the use of larger doses Penicillin has also been administered by continuous intramuscular and intravenous drop particularly in the more resistant infections

At the present time it is the consensus that heparin and dicumarol are unnecessary in the therapy of this condition Although these drugs have been used in combination with penicillin the results with out it are comparable and there is some experimental evidence to show that penicillin alone is equally effective

To enhance penicillin blood levels particularly in resistant cases oral sodium benzoate 2 to 4 Gm (30 to 60 grains) every 2 hours may be administered

2 Streptomycin may be used in cases in which the organism is sensitive to this drug as determined by appropriate laboratory procedures It is administered in the form of intermittent injections the total dose being from 2 to 4 Gm daily (0 5 to 1 Gm four times daily) There is a tendency at the present time to reduce the total daily dose of streptomycin to avoid complications of this therapy particularly the deafness which occasionally occurs

3 Occasional cases of subacute bacterial endocarditis may not respond to either penicillin or streptomycin therapy and after a reasonable period of trial sulfadiazine may be used and is sometimes effective A high blood concentration is desirable and should range from 12 to 14 mg per 100 cc Dosage should be regulated to obtain these blood levels and the use of urea 30 Gm daily frequently adds in maintaining this blood level

4 Supportive measures

a The patient should be confined to bed while febrile

b Occasionally a hypochromic anemia is encountered both because of the patient s disease and sometimes secondary to the sulfonamide therapy This is combated by giving iron ammonium citrates 2 Gm (30 grains) three times a day

c Clinical and in many instances subclinical levels of vitamin deficiency are observed Therefore vitamins A B C and D are given in ample quantities

d During the early stages of the disease the patient may be very ill generally and can only tolerate a very light or even liquid diet However after some response is shown to the therapy instituted a high caloric diet is indicated

e Occasionally the patient s anemia is very severe or the patient may be unusually toxic. In these instances multiple small transfusions may be of great benefit However one should remember to alkalinize the subject before giving such a transfusion This may best be accom

plished by giving 400 to 600 cc of 6/M sodium lactate solution intravenously twice a day for two days prior to transfusion

f Triweekly doses of crude liver extract 2 cc intragluteally have been found to improve the production of blood by stimulating the hematopoietic centers

PERICARDITIS

There are three principal forms of acute pericarditis (1) The rheumatic which embraces the fibrinous and serofibrinous (2) the suppurative which may be due to rheumatic fever, pneumonia streptococcal or gonococcal infections or other diseases and (3) the terminal form occurring in patients dying of uremia These three types of pericarditis are not really separate and distinct diseases but may be considered as stages of one pathological process If the patient survives the acute phase healing takes place and causes connective tissue adhesions between the parietal and visceral pericardial layers and chronic or constrictive adhesive pericarditis develops

Etiology and Pathology The main cause of acute pericarditis is an infection particularly rheumatic fever It may be a direct extension of inflammation from the surrounding organs or through the blood stream in general septic processes Of the acute forms the suppurative is the most serious type it develops as a sequel to conditions as pneumonia empyema or septicemia Often the acute fibrinous or serofibrinous types develop and run a comparatively benign course terminating with complete resolution without the true condition being recognized or diagnosed Frequently the general infection of the preexisting disease may be so severe that the pericardial lesion is completely overlooked It must be kept in mind that acute coronary thrombosis may be an immediate cause of acute pericarditis but in this case the true nature of the underlying lesion is usually recognized Tuberculosis too is a very common cause of pericarditis but needs no description here because it is a chronic form of the disease

Pathologically the pericardium shows inflammation of a serous membrane and the heart is shaggy in appearance due to the thick fibrinous deposits on the visceral and parietal layers

Signs and Symptoms The chief symptom of pericarditis is precordial distress This pain is seldom severe in nature but usually takes the form of a dull aching sensation over the lower portion of

the sternum which is made worse by pressure on the sternum Rapid pulse fever and an increased respiratory rate are practically always present After the pain has persisted for a day or two it often decreases gradually and finally disappears entirely Freedom from precordial pain is usually followed by distressful dyspnea When the pain gives way to shortness of breath it is usually a sign that the precordial effusion has become great enough to separate parietal from the visceral layers of the pericardial sac which relieves the pain This effusion may be mild moderate or severe and the degree of dyspnea is usually dependent upon the amount of effusion Usually dyspnea lasts for a few days and then disappears However this does not mean that the effusion has ceased since it may persist for a much longer time Ordinarily the effusion completely vanishes within a period of a week or ten days although sometimes suppuration may set in which precipitates a serious complication With the disappearance of the effusion the half forgotten pain of the earlier stage may return to some degree together with the classical pericardial friction rub

On inspection one usually finds some characteristic features of acute pericarditis The patient with an acute rheumatic infection who has been progressing fairly well let us say becomes more restless than usual the temperature rises to a higher point the pulse increases in rate and sometimes a dusky cyanotic tinge appears Palpation of the precordial area may reveal fremitus friction On percussion in the early stages no abnormality is found Auscultation brings out the characteristic to and fro friction rub that is not synchronous with either the systolic or diastolic phases of the heart rhythm This friction sound is usually distinguished first over the base of the heart in the region of the great vessels The scratching grating pericardial friction sound differs from an endocardial murmur as follows

1 It is more superficial and appears to lie directly under the skin

2 It does not synchronize exactly with either systole or diastole but as a rule overlaps portions of both

3 A murmur tends to remain unchanged for comparatively long periods of time while the pericardial rub varies in intensity position in the cardiac cycle and location in the precordium almost from day to day

4 The friction rub varies with the respiration It may become louder on inspiration and softer on expiration

When effusion takes place the friction sound becomes less marked and the heart sounds are muffled The apex beat may be displaced to the left and on percussion decided increase of the cardiac dullness is heard This area of dullness takes a conical shape that is the apex of the cone is situated at about the level of the second rib and the base is in the region of the fifth or sixth intercostal space It is during this stage of effusion that the heart muscle may become weaker and fail The failure is not always due to the pericardial effusion entirely since there may be an accompanying myocarditis which weakens the already overburdened heart Another physical sign of pericarditis is the pulsus paradoxus Although this is rarely present sometimes it is an outstanding feature of the examination A pulse that tends to become faint during inspiration and return to its full bounding quality during expiration is the pulsus paradoxus

Diagnosis The diagnosis of acute pericarditis is commonly easy to make This is especially so when the characteristic friction rub occurs The concomitant changes as the pulse rate respiratory rate and fever are helpful Of particular value is the sudden change in the appearance of the patient When in doubt an x ray examination will serve to confirm or repudiate the tentative diagnosis Approximately 300 cc of pericardial fluid is to be present before pericardial effusion can be recognized by x ray examination Usually at least 500 cc is necessary for recognition by physical findings

Prognosis The prognosis as a whole depends to a great extent upon the immediate cause as the simple pericarditis with or without effusion of rheumatic variety usually resolves and the patient recovers Of course chronic adhesions may be the result of the acute pericarditis and they may ultimately be the cause of the patient s premature death The amount of effusion is a fairly good prognostic guide the greater the effusion the worse is the outlook for the patient Purulent pericarditis is especially dangerous because it develops in the course of diseases of a serious nature as pneumonia empyema and septicemia but these cases are not always hopeless

TREATMENT

1 Absolute rest in bed is imperative until the period of fever and complications has passed

2 The antecedent disease if recognized should be treated as vigorously as possible

3 As pain may be a distressful feature especially in the early stages small doses of pantopon 20 mg (⅓ grain) morphine 10 mg (1/6 grain) codeine 60 mg (1 grain) or dilaudid 2 mg (1/32 grain) may be given hypodermically for relief when necessary

4 Icebags over the precordium give more relief than heat

5 The irritating painful cough which is often a complication calls for codeine sulfate 16 mg (¼ grain) in some vehicle as simple syrup given as needed

6 Metrazol or cardiazol quinine may be given if blood pressure is low or when premature beats or paroxysmal tachycardia are present

7 The intake of fluid should be limited to about 1000 cc (1 quart) per day

8 Diuretics as mercupurin or salyrgan 1 cc intravenously every other day for three doses or diuretin 0 6 Gm (10 grains) three times a day should be given to relieve the pressure of the effusion

9 As long as the effusion is well borne by the patient aspiration of the pericardial sac is not necessary If a massive effusion is present and the patient becomes extremely dyspneic cyanotic and weak the needle should be introduced at the fifth or sixth intercostal space just to the left of the left sternal border or in the sixth intercostal space outside the nipple line Needling however has become a rare event in my experience The question of paracentesis of the pericardial sac is often brought up but it should be rarely resorted to because the effusion usually absorbs and seldom causes enough embarrassment to warrant the introduction of a needle When heart failure comes on in the presence of effusion I am of the opinion that it is due not so much to the effusion as to the myocardial and endocardial involvement

10 The general management of the patient requires consideration of the proper amount of food and vitamins in the diet

11 As anemia is often present good sized doses of iron ammo-

nium citrate 2 Gm (30 grains) three times a day or some other iron preparation should be given daily

12 If purulent pericarditis is present a surgical opinion should be sought regarding the removal of pus Although purulent pericarditis may resolve without surgical drainage an operation proves to be the most effective measure in the treatment of these cases

13 Pericarditis due to pneumococcus or streptococcus infections or bacteria which respond to the sulfonamides or penicillin requires *these therapeutic measures given in the usual manner* If pericarditis is rheumatic in origin the full therapeutic regimen for this condition may be employed

CHAPTER VII

The Heart

(Continued)

RHEUMATIC FEVER

Rheumatic fever is an acute infectious disease of unknown etiology causing fever and a marked intoxication characterized by the presence of minute focal proliferative lesions in the heart and other tissues and organs

Etiology Rheumatic fever is usually found in the temperate climates particularly in cold damp areas during the winter and early spring It has a tendency to appear in epidemic form at irregular intervals occurring most frequently in children between the ages of 5 and 15 years However several epidemics have been reported in the armed forces particularly among the younger servicemen In these large series of cases rheumatic fever proved a highly communicable disease frequently preceded by an outbreak of upper respiratory infections

Although the cause of rheumatic fever is not known definitely more and more evidence points to the Hemolytic streptococcus group A as the source of the anaphylactic reaction The disease often follows Hemolytic streptococcus infections of the upper respiratory tract although more than one strain of streptococci may be demonstrated in a patient The portal of entry is probably the throat Other suggested etiologic factors are an allergic or a humoral phenomenon Trauma is believed to play a role in the disease since a joint injury may serve as the site of an initial lesion Environmental factors such as exposure to cold and dampness fatigue and crowded living conditions are also considered important in the development of rheumatic fever Other predisposing factors that have been considered are pharyngitis sinusitis and tonsillitis Rheumatic fever is usually the result of repeated infections with renewed activity in old foci of infection

Pathology The affected joints show edema of the periarticular tissue and the synovial cavities have a thick yellow fluid which con

tains relatively large amounts of fibrin The synovial membrane is thickened and injected and the cartilage of the joint may be eroded The body cavities as the pleural and pericardial cavities may also contain a serofibrinous fluid The pericardial epithelium may be destroyed and obliterative pericarditis may ensue with organization of the exudate Endocarditis or valvulitis in the early stages show minute gray pink vegetations along the line of approximation of the cusps with some thickening The mitral valve is most commonly affected *The Aschoff bodies which are to rheumatic fever what tubercles are to tuberculosis* occur about the smaller blood vessels as a small necrotic area surrounded by polymorphonuclear leukocytes and cells with a large basophilic cytoplasm with large frequently multiple nuclei These large basophilic cells are found in all the acute lesions

Signs and Symptoms The symptoms of sore throat or upper respiratory infection are the most prominent early manifestations of the disease accompanied by general malaise fatigue pallor anorexia fleeting pains in the limbs and persistent loss of weight A sense of coldness associated with clammy sweat and exhaustion is also evident as well as a rapid pulse and a swift rise in temperature ranging within 24 hours between 39° and 40° C (102° and 104° F) This fever lasts for 10 to 15 days Associated with these clinical features are marked prostration profuse sweating arthritis and painful joints that are tender swollen hot and red While the involvement is transitory and migratory with the large joints being involved individually or severally the joints most subject to strain are the first to be affected Each joint may be inflamed for a period of one to 6 days and relapses may occur

Clinical signs of cardiac involvement are present in more than 50 per cent of cases and it is probable that the heart is affected in almost every case The chief signs of myocarditis during the acute period are enlargement of the cardiac area disturbances of rhythm and rate and electrocardiographic changes There is an increase in heart size due to the acute cardiac dilatation and the murmurs which are present may be due to a relative insufficiency of the valves Precordial pain and hyperesthesia are suggestive of cardiac involvement and a palpable diffuse apical impulse with a gallop rhythm confirms this suspicion An accentuated third sound dropped beats and pre

mature contractions are frequently noted The development of pericarditis in a patient with signs of valvular injury signifies pancarditis Friction rub is diagnostic of pericarditis With pericarditis there is an effusion in the pericardial sac tachycardia and increasing dyspnea and cough The most consistent electrocardiographic change is prolongation of the P R interval which may be the only indication of heart involvement and which is usually transient Partial A V heart block and auricular ventricular dissociation occur less frequently

Subcutaneous nodules in the skin are specific and important signs of a severe virulent infection Central nervous symptoms may be those of chorea in children while in adults there is usually delirium and coma if this system is involved

There is a rapidly progressive secondary anemia with a leukocytosis ranging from 10 000 to 25 000 cells with a shift to the left Erythrocytes and hemoglobin are reduced and the sedimentation rate is always rapid The urine is scanty highly concentrated and may show a trace of albumin and many red and pus cells Acute nephritis is an unusual but serious complication of acute rheumatic fever

Diagnosis The diagnosis is made on the clinical phenomena previously described and should be strongly suspected in any case of acute migratory polyarthritis It has been suggested by Jones that the following criteria be adhered to in diagnosis (1) Any combination of any two of the major manifestations such as arthralgia carditis chorea nodules and a history of previous rheumatic fever (2) a combination of at least one of the major manifestations with two minor manifestations such as fever abdominal or precordial pain erythemas epistaxis pulmonary changes and laboratory abnormalities (3) the presence of rheumatic heart disease increases the diagnostic significance of the minor manifestations when no other cause for these exists

Differential Diagnosis Rheumatic fever must be distinguished from the following

1 Multiple acute secondary arthritis which is differentiated from acute rheumatic fever by the purulent infection of the joints

2 Gonorrheal arthritis which is usually quite readily distinguished because of the presence of a genital infection

3 Acute osteomyelitis and septic arthritis in which cases there

tains relatively large amounts of fibrin The synovial membrane is thickened and injected and the cartilage of the joint may be eroded The body cavities as the pleural and pericardial cavities may also contain a serofibrinous fluid The pericardial epithelium may be destroyed and obliterative pericarditis may ensue with organization of the exudate Endocarditis or valvulitis in the early stages show minute gray pink vegetations along the line of approximation of the cusps with some thickening The mitral valve is most commonly affected The Aschoff bodies which are to rheumatic fever what tubercles are to tuberculosis occur about the smaller blood vessels as a small necrotic area surrounded by polymorphonuclear leukocytes and cells with a large basophilic cytoplasm with large frequently multiple nuclei These large basophilic cells are found in all the acute lesions

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4 Vitamins A B C and D are useful in building up the general resistance of the patient If a dietary deficiency exists or if a patient has been seriously ill vitamins are especially indicated

5 Iron therapy is indicated for the secondary anemias late in the course of the disease Ferrous sulfate Gr 6 t i d may be given

6 Salicylates are indicated to relieve abdominal symptoms precordial pain joint pain and fever Although the salicylates have an analgesic and antipyretic action in rheumatic fever it is generally agreed that they have no effect on the actual disease process Neither do they prevent recurrences of the disease

Clinical response to large doses of sodium salicylate 10 Gm daily is rapid but salicylism is a possible consequence A suggested schedule of dosage of either sodium salicylate 1 7 Gm (25 grains) or acetylsalicylic acid with sodium bicarbonate 1 3 Gm (20 grains) orally every 4 hours around the clock may be used In the event that gastrointestinal distress may appear sodium bicarbonate 1 3 Gm (20 grains) or potassium bicarbonate is administered orally with every dose of salicylate The blood salicylates reach the optimal level of 350 to 500 micrograms per 100 cc of blood in 24 to 48 hours The blood level may be maintained by regular administration of salicylates together with an adequate amount of water 3000 cc daily Oral administration of salicylates is preferred over intravenous administration In the few cases where salicylates cannot be given by mouth 10 Gm of sodium salicylate in 1000 cc of 0 9 per cent sodium chloride is administered by intravenous drip in four to six hours This is given daily for one week and if a satisfactory response takes place oral therapy replaces intravenous therapy When using intravenous salicylates evidences of salicylism must be closely watched for The effect of the salicylates may be increased by giving magnesium carbonate in amounts equal to the dosage of salicylate

7 Immobilize the joints A soothing liniment or ointment such as methyl salicylate is applied to the involved joints after which they are wrapped in warm flannel Aminopyrine has been used in doses of 2 to 3 Gm (30 to 45 grains) with good results Some authors feel that a patient can tolerate this drug in combination with digitalis far better than with the salicylates However it must be given with care since agranulocytosis may follow its use If the fluid in the joint space

are a septic fever profound intoxication and marked leukocytosis

4 Gout in which the history and presence of a high blood uric acid make the diagnosis quite simple

5 Tuberculosis brucellosis and trichinosis

6 Abdominal symptoms including pain tenderness rebound tenderness and cramps may indicate the onset of rheumatic fever and the diagnosis may be confused with that of appendicitis

Prognosis Once rheumatic fever has become advanced prognosis becomes worse although in the acute attacks in patients without previously damaged hearts mortality is set at between 1 and 4 per cent

TREATMENT

Treatment of rheumatic fever is still largely symptomatic Its aim is to control infection and to prevent complications particularly heart damage Since serious rheumatic heart disease results not from the first attack but from a succession of relapses and recurrences treatment is prolonged and prevention of further rheumatic activity is of paramount importance The treatment roughly may parallel the two stages of the disease active and quiescent During the active stage the following regime is beneficial

1 Bed rest preferably in a hospital is instituted in any case with a persistent infection and the individual is kept completely at rest until all evidence of infection has subsided *i e*, until heart rate white blood count Schilling count and sedimentation rate have been normal for some time Special attention is paid to temperature pulse changes in heart size and development of bruits As the condition improves the patient is allowed to sit up gradually and slight diversionary activity is permitted with the pulse rate being watched carefully Such prolonged confinement which may extend into months is often difficult to achieve as the acute symptoms may subside and the patient feel well long before the disease has run its course However since heart damage may be minimized or prevented in this manner it is well worth while

2 Protect the patient from cold and chilling

3 The diet should be high in calories and contain easily digestible food A liberal fluid intake is recommended to combat or prevent dehydration except in the presence of edema when fluid intake is restricted

Health Department establish institutions for the care of rheumatic fever victims as it has for tuberculosis Removal to a warm tropical climate is both expensive and unnecessary since rheumatic fever occurs even in the tropics

2 The proper balance must be struck between exercise and rest In general moderate activity in a good environment and under careful supervision is satisfactory Plenty of rest and a long after noon nap are recommended The patient should not return to school for 6 to 8 months after the disease is quiescent but he may try to continue his scholastic activity during convalescence

3 When the child returns home convalescence should be con tinued if the situation requires it It is best for the rheumatic in dividual to have a separate bedroom avoid crowds and observe the other precautions necessary to prevent an upper respiratory tract in fection If he develops any infection no matter how slight he should go to bed The diet should be adequate with plenty of milk and citrus fruit

4 It is in prophylaxis that the sulfonamide drugs play their important role in the therapy of rheumatic fever Daily administra tion of small doses of sulfathiazole or sulfadiazine will reduce the incidence of streptococcal infection by 80 per cent In this way the drug lessens the frequency of primary or recurrent attacks of rheumatic fever Penicillin in pastules may in the near future be used in the prophylaxis of acute hemolytic streptococcal infections but this therapy does not lessen the rate of occurrence or recurrence of rheumatic fever The salicylates offer no protection from recur rences Since the etiology of rheumatic fever is still uncertain it is difficult to discover a successful specific prophylactic treatment More and more emphasis has been placed on the public health aspects of the disease and it is felt that a general improvement in housing nutrition and cleanliness would do much to stave off this malady

LUPUS ERYTHEMATOSUS

Lupus erythematosus may be defined as a systemic disease with a specific type of cutaneous manifestation This syndrome is not a new disease but rather an old disease with a new name having been de scribed by Olser 50 years ago He pointed out that without the skin manifestations the diagnosis was almost impossible to make

is large in amount it is aspirated using careful technic to prevent the introduction of any infection

8 Aspirate the fluids in the heart sac and pleural cavities

9 Morphine sulfate, 10 mg (1/6 Gr) or codeine sulfate 32 mg (1/2 Gr) may be necessary for the relief of pain

10 Digitalis is indicated only in cases of heart failure but it must be used carefully In treating the heart failure of rheumatic fever it may be more important to promote diuresis than to regulate the heart rate In congestive failure the condition may be controlled by the xanthines If they are not effective digitalis may be used and as a last resort the mercurial diuretics

11 The sulfonamides have proven valueless in the treatment of rheumatic fever *per se* Although the drug does not relieve symptoms and may enhance them it may help remove intercurrent foci of infection and prevent the untoward effects of rheumatic fever Sulfonamide therapy may be combined effectively with salicylate therapy The suggested dosage is sulfanilamide or sulfadiazine 1 to 2 Gm (15 to 30 Gr) every four hours for several days and then salicylate therapy only

12 Remove all foci of infection when the disease becomes quiescent In general it is best to wait six to eight weeks Then operation should be performed whether or not healing has occurred since it is probable that the disease will not disappear until the infection is removed However some physicians believe it is best to wait six months before removing foci of infection First because of the difficulty in determining when the disease becomes quiescent second because of the frequency of recurrences of the active phase of the disease following operation

13 Oxygen may be of inestimable value in the treatment of such complications as rheumatic pneumonitis and congestive failure Early and prolonged administration of oxygen by the nasal tube method will relieve restlessness cyanosis dyspnea and in some cases tachycardia

During the quiescent stage of the disease the following points must be taken into consideration

1 Prolonged convalescent care is necessary to prevent relapses and remissions The child is best treated in a sanitorium or convalescent home and it has often been suggested that the Public

acteristics of a septic process The urinary findings indicate an inflammatory process in the kidneys

Diagnosis The diagnosis of lupus erythematosus is made by a process of exclusion and may be suspected when a patient has an unexplained fever supplemented by the other features mentioned above such as anemia splenomegaly and pleural or pericardial or peritoneal effusions When the obscure fever and these other features are associated with the specific type of butterfly lesion involving the nose and the cheeks the diagnosis is almost certain Blood cultures are practically always negative Thus the skin lesion which may be present before the onset of the constitutional symptoms or which may develop during the symptoms points the way to a diagnosis

Prognosis While many cases of lupus erythematosus may be characterized by mild systemic reactions and prolonged remissions the prognosis in the acute form is almost always fatal and death may occur in from 2 months to 4 years

TREATMENT

The chief point of treatment is in prevention and any factors such as *exposure to sun rays burns trauma and infections that might* cause the acute phase of the disease should be avoided In addition the following should be tried

1 Absolute bed rest

2 *Quinine sulfate 30* mg (½ grain) orally three times a day and increased up to 0 12 Gm (2 grains) three times a day to bring relief and prolong life

3 Bismuth 0 03 Gm (1/3 of a 2 cc ampule) given intramuscularly twice or three times weekly to prolong remissions The drug is absolutely contraindicated in the acute and in the active phases of the subacute form

4 Heat applied to the painful joints and muscles

5 Blood transfusions to combat the anemia These however may have no beneficial influence on the primary disease process

COR PULMONALE

Cor pulmonale is a disease of the heart terminating in right ventricular failure that is caused by obstruction to the flow of blood through the pulmonary vessels It may be divided into two forms the acute and chronic

Etiology and Pathology Lupus erythematosus is a disorder of unknown cause although it is commonly believed to be due to a septic infection in a previously sensitized individual The disease occurs predominantly but not exclusively in women varying in age from 20 to 50 The discoid or localized type which is also the chronic phase of the disease may be present for many years causing little or no discomfort However it is the discoid chronic type of skin lesion which becomes aggravated on exposure to sunlight after trauma or during an acute infection This appears to be the starting point of the subsequent generalized disseminated acute lupus erythematosus However lupus erythematosus may develop without any skin manifestations before the onset and the skin lesions may develop during the course of the acute episode

Nearly all of the internal organs as well as the skin may become involved The blood forming system becomes depressed and leukopenia anemia and thrombocytopenia follow The kidneys become the site of a chronic toxic process which produces some of the features of glomerulonephritis but which fails to develop the classical picture of chronic glomerulonephritis later on *The heart is of special importance as in many cases a non* bacterial endocarditis occurs as a part of the disease Libman and Sacks gave a special description of this type of endocarditis which *is now known as the Libman Sacks syndrome It is however only* one of the visceral manifestations of a widespread disorder affecting nearly all of the tissues of the body The reticulum fibers of the body may become swollen increased in number and edematous This characteristic has given rise to the opinion that lupus is a constitutional disease of the supporting fibers of the entire body

Signs and Symptoms The characteristic sign in a typical case is the rapidly spreading butterfly erythematous patch across the nose that has developed from a skin lesion aggravated by exposure to sun light after trauma or during an acute infection Lupus may develop however without any skin manifestations before the onset and the skin lesions may develop during the course of the acute episode

Symptoms of tiredness loss of appetite weakness and joint and muscle pain develop gradually followed by an abrupt acute phase with fever severe anemia splenomegaly leukopenia and other char

time it has been present Dyspnea cough cyanosis and weakness may have been present for long periods of time as the result of the pulmonary disease As these same symptoms may represent early cardiac failure, it is frequently difficult to determine where the cause terminates and the effect begins This difficulty is made more severe because of the long chronic course of the pulmonary process and the usually insidious onset of cardiac weakness and failure Such a combination frequently causes the transitional period to be over looked by both patient and physician The symptoms become in creasingly severe in proportion to what would be expected from the pulmonary process alone With the onset of definite right heart failure symptoms and findings produced by congestion of the liver edema of the lower extremities and passive congestion of the neck veins become manifest Rales in the lungs and tachycardia too may have been present for a long time previous to the onset of cardiac involvement but with congestive failure these findings become more marked The heart may not show definite right sided enlargement until relatively late but earlier in the course of the disease accentua tion of the second pulmonic sound occurs and evidence of right ventricular enlargement is present Clubbing of the fingers and toes is frequently seen

Diagnosis Diagnosis of acute cor pulmonale is established by the recognition of the clinical picture of pulmonary embolism and by the presence of a source of emboli In chronic cor pulmonale the diag nosis depends on the presence of the preexisting underlying pulmo nary disease and evidence of right ventricular failure

Common findings are elevation of the red blood count and hemo globin The electrocardiogram may show right axis deviation and right ventricular strain Enlargement of the right ventricle may be difficult to show with x rays as this chamber lies anteriorly but a prominent pulmonary artery is seen on the left cardiac border On the right anterior oblique projection increased prominence of the right outflow tract may be observed Enlargement of the right auricle is demonstrated with a flat film of the chest or with a barium esopha gram In the later stages the heart may show generalized enlargement

Prognosis The course is variable but usually follows that of the underlying pathology As the underlying pathology progresses more strain is thrown on the lesser circulation and on the right ven

Acute cor pulmonale is the result of embolism from phlebothrombosis usually in the legs and its recognition is important because ligation of the thrombosed veins of the leg is likely to be followed by complete recovery Chronic cor pulmonale however is punctuated by acute episodes of right sided heart failure These attacks at times are preceded by exertion and at other times the precipitating factor is obscure Following the early bouts of acute right sided failure, the patient may appear quite well for a time but eventually the heart becomes exhausted from repeated attacks and fails permanently

Etiology and Pathology The pathogenesis of this type of heart disease is extensive and is characterized by long standing disease of the lung parenchyma or of the pulmonary vessels or gross deformities of the thoracic cage with consequent obstruction to the flow of blood through the pulmonary vessels and subsequent compensatory hypertension in the lesser circulation The pulmonary hypertension produces strain on the right ventricle This if long-continued leads to hypertrophy dilatation and eventual failure of this chamber through a process of fatigue rather than degenerative changes Such hypertension in the lesser circulation and its effect on the right ventricle are comparable to hypertension in the systemic circulation with its corresponding effect on the left ventricle Apropos of this it should be borne in mind that the texture of the right ventricle is more delicate than that of the left

The etiology of the underlying pulmonary disease may be quite varied It must be extensive enough to interfere with the free flow of blood through the pulmonary vascular bed and it must be present over a long period of time Among such causes are (1) silicosis (2) pulmonary fibrosis due to any chronic inflammation of the lungs as chronic bronchitis bronchiectasis and fibroid tuberculosis (3) asthma and resulting emphysema, (4) long standing pulmonary atelectasis (5) marked scoliosis or kyphosis or any gross deformities *of the thoracic cage sufficient to diminish the oxygenating capacity* of the lung (6) Ayerza s disease (7) Pick s disease with extensive adhesions involving the mediastinum (8) emphysema from any cause and (9) pulmonary arteriosclerosis

Signs and Symptoms The signs are variable and depend on the nature of the underlying pulmonary disease and the length of

thrombosis in the large veins of the leg pelvis or abdomen from vegetations on the valves of the right side of the heart or from thrombotic masses in the right auricle that develop when heart failure and auricular dilatation occur Although other causes occasionally are recorded those noted above account for the majority of cases Pulmonary embolism from blood clots in the large veins of the leg is most common and develops especially after abdominal or pelvic operations or fracture of the leg The incidence of pulmonary embolism has been estimated as follows by Neuhof and Klein From 0 1 to 0 2 per cent of all operations 2 per cent of all deaths including posttraumatic postoperative postpartum and medical 6 per cent of postoperative deaths and approximately 10 per cent of all autopsies

Structurally there are three pathological changes seen with this condition

1 The group in which the embolus is so large that it plugs one of the main branches of the pulmonary artery or even the main artery itself In these cases sudden collapse and death usually occur within five minutes

2 Those which result from an embolus that obstructs a medium sized artery of the pulmonary tree A large area of infarction develops as a result of this arterial plug and the sudden shock dyspnea cyanosis pain in the chest and other signs commonly attributed to pulmonary embolism develop In this type the embolism may be fatal but resolution and recovery are common

3 That kind characterized by the lodging of numerous small emboli which occlude some of the smaller and smallest branches of the pulmonary arterial tree small areas of hemorrhagic infarcts varying in size from a pea to a hickory nut develop as a result This is the kind of pulmonary embolism that is frequently confused with pneumonia

Signs and Symptoms The signs and symptoms of pulmonary embolism depend largely on the size of the artery obstructed by the embolus A small embolus in a small artery of the lung may not produce an infarct large enough to cause any characteristic features larger emboli may obstruct larger arteries and cause serious manifestations

Obviously the signs and symptoms of pulmonary embolism vary greatly depending upon the size and position of the obstructing mass

tricle until failure finally occurs During the process of the disease, the reserve of the right heart is diminished and the heart becomes less able to withstand added burden that might be imposed upon it An example of such an added burden is acute respiratory infection to which these patients are subject particularly during the winter months Cardiac decompensation is common during such infections True pneumonia is a burden which few are able to withstand

TREATMENT

In the treatment of acute cor pulmonale

1 An immediate attempt is made to find the thrombosed vein responsible for the acute pulmonary embolus If the thrombosis is located ligation of the veins of one leg or both legs may be necessary to prevent future embolism

2 Dicumarol or heparin or both have been recommended

3 Pantopon grains 1⁄3 (0 020 Gm) or morphine sulfate grains 1⁄4 (0 015 Gm) combined with 1⁄100 grain of atropine sulfate is given subcutaneously

4 Papaverine hydrochloride grains 3 (0 195 Gm) may be given intramuscularly or intravenously every three hours for six doses The same dosage by mouth is continued for a number of days

5 Oxygen may be necessary

6 If there is evidence of right ventricular failure digitalization with a purified glycoside or digitalis leaf may be effective

In the chronic type of cor pulmonale treatment is aimed at the failure of the right ventricle Venesection digitalis papaverine and oxygen are the chief remedies employed Diuretics may be helpful

PULMONARY EMBOLISM

Luisada defines pulmonary embolism as a sudden obstruction of the pulmonary artery one of the stems or one or more secondary branches by one or more emboli which may arise in the right heart or in any part of the systemic venous circulation with the exception of the portal system

This syndrome s importance lies in its serious significance and in its preventability for it involves the great vessels and is an intra thoracic disease simulating or complicating heart disease itself

Etiology and Pathology Pulmonary embolism may arise from

TABLE I

POSTOPERATIVE VENOUS THROMBOSIS AND PULMONARY EMBOLISM

Number of operations	172 888	
All thrombosis and embolism	1665	0 96%
Pulmonary embolism	897	0 52%
Fatal pulmonary embolism	343	0 20%
Thrombophlebitis	938	0 54%

TABLE II

PREDISPOSING CONDITIONS

		None	*Cardiac*	*Peripheral Veins*	*Blood*	*Carcinoma*	*Severe Infections*
Men	757	276/36 5	126/16 6	77/10 2	163/21 5	224/29 6	223/29 5
Women	908	303/33 4	93/10 2	172/18 9	307/33 8	190/20 9	156/17 2
Total	1665	579/34 8	219/13 15	249/14 9	370/28 2	414/24 9	379/22 8

TABLE III

LOCATION OF POSTOPERATIVE VENOUS THROMBOSIS

Veins lower extremity	1199	85 6
Veins abdominal viscera	116	83
Inferior vena cava	39	2 8
Veins upper extremity	24	1 7
Veins head and neck	17	1 2
Superficial veins trunk	6	0 4

are similar Nevertheless a consideration of the following diagnostic criteria will aid one in the differential diagnosis

In favor of pulmonary embolism is a sudden onset of the disease in a bedridden patient or a postoperative convalescent of either sex Clinically chest pain that is sharp and pleuritic but has no typical localization may appear as well as intense dyspnea venous congestion cyanosis hemoptysis and shock The heart is usually rapid the blood pressure may be low and fever leukocytosis an increased sedimentation rate and an elevated icterus index are common findings

On the other hand coronary thrombosis has a slightly more gradual onset and occurs in ambulatory patients predominantly among

In general the characteristic signs of a large pulmonary embolism are sudden onset of shock dyspnea pallor and pain in the chest Cyanosis may or may not be present A point that requires emphasis is that pain need not be present

In other forms of pulmonary embolism the vessels plugged are of smaller size and certain physical signs and symptoms are characteristic Physical signs are usually absent during the first 24 hours but after infarction takes place a friction rub rales and alterations in breath sounds as well as impairment of the percussion note are observed X ray examination usually discloses clouding of the costophrenic angle in the lung From the fourth to the tenth day pleural changes take place and the area of cloudiness increases and remains for months but the lung density usually disappears within two weeks

In cases of partial infarction there are no obvious physical signs However if fever is present and suddenly rises at night with pleuritic pain dyspnea cyanosis and a faster pulse rate small incomplete infarctions are probably present

If the physician keeps pulmonary embolism in mind in postoperative cases fractures and heart or infectious diseases diagnosis is not difficult If a patient acquires a fever when convalescence is otherwise satisfactory or if he has a chest pain and signs of pleurisy consolidation or pleural effusion pulmonary embolism is apt to be present In addition the presence of a few or of several of the following symptoms may assist in confirming a diagnosis of pulmonary embolism A weak or rapid pulse a marked fall in blood pressure leukocytosis cold clammy sweat cough and in some cases hemoptysis vomiting tachycardia faintness or syncope and occasionally collapse However bloody sputum and pain are not necessary for diagnosis

Barker and his associates have conducted an extensive survey to determine the incidence of postoperative venous thrombosis and pulmonary embolism Their findings are briefly summarized in Tables I II and III

Postoperative thrombi were commonest following laparotomy on the female pelvic organs where injury to the iliac veins may occur

Differential Diagnosis Pulmonary embolism is especially apt to be confused with coronary thrombosis since the symptoms of the two

1 Oxygen of the 100 per cent variety may be used at the beginning of treatment but after one half or one hour better results are obtained by switching to the customary 40 to 60 per cent oxygen This is best administered with the Boothby type of mask

2 Morphine 16 mg (¼ grain) or pantopon 20 mg (⅓ grain)



Fig 1—Postoperative exercise apparatus to improve venous backflow The patient pedal on this stationary bicycle for five minutes three times a day starting on the third postoperative day (de Takats)

hypodermically may be given immediately to allay mental and physical distress

3 Atropine 0 9 mg (1/75 grain) injected intravenously relieves the vascular spasm of the lung The atropine counteracts the constriction of the smooth muscles of the coronary system caused by irritation of the vagus since it blocks the vagal impulse

4 Papaverine hydrochloride 32 mg (½ grain) may be injected intravenously It is used to release the contracted smooth muscle

males Typical findings are constricting crushing chest pain radiating especially to the left shoulder and mild dyspnea and cyanosis diaphoresis nausea and vomiting Other findings of fever leukocytosis and so on are late phenomena

The electrocardiographic tracings are often not very helpful in differentiating the two conditions because characteristic changes are not always present However the following evidences are frequently seen on the electrocardiogram in pulmonary embolism

1 Deep S in leads I and II giving the picture of right axis deviation

2 Deep Q_3 with a low voltage throughout

3 The S-T_1 and S-T_2 may show a low takeoff and the S-T_3 may be elevated with inversion of T_2 and T

4 Inversion of the T wave of the precordial leads particularly over the right side of the heart may be observed This change regresses with improvement the configuration returning to normal from the left to the right positions

An x ray examination of the chest may not be very helpful because changes may be lacking However it may help in identifying other conditions associated with or confused with embolism Pneumonia pneumothorax massive collapse of the lung and pulmonary embolism all must be taken into consideration in the differential diagnosis

Prognosis Pulmonary embolism is considered an extremely fatal disease and estimates of the mortality while not including small emboli are estimated as high as 30 to 40 per cent

TREATMENT

The treatment of pulmonary embolism requires prompt and decisive action *When the patient is first seen the distress from dyspnea pain in the chest and mental anxiety is very pronounced* Usually the patient will be sitting up in a semireclining position panting *for air unless he is too collapsed to do so* In either case the expression on his face fear mingled with pain serves to convince one that a catastrophic event has just occurred Any emergency treatment *must* be administered carefully because of the possibility of a mistake in diagnosis

The treatment then may be outlined briefly as follows

1 Oxygen of the 100 per cent variety may be used at the beginning of treatment but after one half or one hour better results are obtained by switching to the customary 40 to 60 per cent oxygen This is best administered with the Boothby type of mask

2 Morphine 16 mg (¼ grain) or pantopon 20 mg (⅓ grain)



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4 Papaverine hydrochloride 32 mg (1/ grain) may be injected intravenously It is used to release the contracted smooth muscle

Atropine and papaverine are given three times daily in the above amounts After the continuation of the intravenous injections of these drugs for two or three days copavin 64 mg (1 grain) may be given three or four times a day by mouth for a week or two in addition to the above

5 Prophylactic measures are taken on patients who are candidates for future embolism Those with phlebothrombosis thrombophlebitis varicose veins heart disease and those undergoing surgery

a Various measures are advocated to combat sluggish venous circulation while the patient is confined to bed Frequent changes of position *elevation of the foot of the bed application* of heat to the legs compression bandages deep breathing exercises passive and active leg exercises and early postoperative rising

b The maintenance of fluid balance is important in prophylaxis since a dehydrated patient has a slow circulatory rate Physical and chemical changes in the blood may be caused by dehydration resulting not only from an inadequate fluid intake but also from vomiting diarrhea sweating and hemorrhage A record of fluid intake and output will assist in maintaining the fluid balance

c Anticoagulant therapy with heparin and/or dicumarol is begun postoperatively These drugs will prevent formation of intravascular clots but they will not dissolve clots already formed Combined heparin dicumarol therapy is advocated heparin for the immediate effect and dicumarol later

6 Surgical procedures are indicated in serious cases For example if embolism has occurred before in a patient with phlebothrombosis and if the patient is past 50 Ligation of the vein of the leg proximal to the thrombus is a simple safe procedure and an assurance against recurrence of the thrombus and occurrence of an embolus

CHAPTER VIII

Metabolic Disorders

DIABETIC COMA

The most important factor in diabetes is that diabetic coma may develop and kill the patient Therefore the greatest responsibilities of the physician are to safeguard the patient from coma and to save him if coma occurs Although diabetic coma does not occur as frequently as formerly it continues to be a significant factor in the treatment of diabetes Diabetes is a common disease usually benign and it is often treated too lightly by the patients themselves and occasionally by the physician in charge It has long been known as a disease of complications and until some complication arises the disease may be almost entirely overlooked since it may cause no distress

Etiology Diabetic coma is usually precipitated by (1) an excessive amount of food and particularly the wrong kind of food (2) interruption in the use of insulin or too little insulin and (3) infections Some diabetic patients deliberately break their diet and consume an excessive amount of carbohydrate food if the insulin is omitted coma is almost always the rule The interruption of insulin is becoming a less common occurrence due to the campaign for education of these patients One of the common reasons for the omission of insulin is the development of an upper respiratory infection or an acute digestive disturbance which interferes with the patient s eating the regular diet Frequently these patients believe that if they do not eat their regular portions of food the insulin becomes unnecessary They fail to realize that in case they do not take food by mouth sugar is called up from the glycogen stores of the body and this glucose must be burned just the same as the glucose from ingested food Of the three common conditions that precipitate coma probably infections head the list It is not necessary that the infection be a very severe one for a simple type as acute tonsillitis acute bronchitis acute gastroenteritis carbuncle boil pneumonia or hepatitis which may be a relatively benign condition in a normal person is

serious in a diabetic It interferes with the metabolism of the body and disrupts the balance that the diabetic patient has maintained by exercise diet and insulin Any infection must be looked upon as an important matter because it may produce coma in a diabetic

Owing to the inadequacy of insulin production disordered carbohydrate and disordered fat metabolism occur and thereupon there follow two events which are of major importance in the production of coma First there is an accumulation of ketones in the body and these produce dehydration by their diuretic effect Secondly there is a distortion of the normal acid base balance toward the acid side If the process is allowed to continue unchecked the buffer systems of the body are no longer able to compensate and clinical acidosis appears Normally the body helps to maintain its acid base equilibrium through two methods The dissociation of sodium bicarbonate to carbon dioxide in the lungs and the formation of ammonia in the kidneys Under conditions of diabetic acidosis there is a breakdown of the ammonia production mechanism and there follows a loss of fixed base through the kidneys in the form of sodium as well as ammonium salts

Signs and Symptoms One of the difficulties with diabetes is that it appears so gentle and innocuous Yet it is a disease that is ready to strike when the proper moment arises and unless one is on the alert for its complications including coma the patient may lose his life The development of diabetic coma is frequently rapid and its duration is sometimes difficult to fix After coma sets in the patient rarely lives more than a few days and death may take place within a few hours if treatment is not instituted immediately

The signs and symptoms of diabetic coma have been for convenience sake divided into the precoma and coma phases In the precoma stages the patient has already begun to suffer from the symptoms of ketosis It is important to recognize this promptly and to be on the lookout for the clinical features of acid intoxication which if left unchecked produce diabetic coma It is not enough for the physician to know these evidences of oncoming disaster the patient must be educated so he too will realize the significance of the early signs and symptoms They are as follows

1 Excessive thirst
2 Vomiting

3 Headache nausea apathy and weakness

4 A feeling of general malaise with aches and pains in the joints or abdomen

5 Respiratory distress brought on by slight exertion which previously caused no difficulty

6 A tendency for the patient to be tired sleepy restless or nervous

Many of these symptoms may develop early in the stage of acid intoxication The speed with which diabetic coma evolves depends on the severity of the metabolic disturbance which is present The treatment is the most important factor

The line of demarcation between the stage of precoma and coma is often difficult to draw From the practical point of view the treatment is almost essentially the same in both stages Whenever a diabetic develops any one of the features mentioned above the urine should be carefully checked for sugar acetone and diacetic acid The test for diacetic acid is the most important of all and will be discussed under the heading of diagnosis

The onset of coma is merged gradually with the precomatose symptoms Vomiting excessive thirst and somnolence going over into complete unconsciousness are the clinical evidences of coma The mental depression that occurs with coma states in diabetes has not been adequately explained Theoretically at least the causes thereof may be attributed to one or more of the following Accumulation of ketone bodies more specifically acetoacetic acid which have been supposed to be toxic to nervous tissue dehydration and finally loss of base

As coma becomes more firmly established the clinical picture is more or less constant One may say that diabetic coma is made up of two main syndromes dehydration and ketosis While both merge to produce a classical clinical picture of coma the separation may be helpful from the standpoint of treatment

1 The dehydration syndrome
   - *a* The skin is dry and inelastic
   - *b* The face is flushed and drawn but fever is absent
   - *c* The mouth is dry and the tongue is red beefy and coated
   - *d* The pulse is weak and its volume reduced
   - *e* The blood pressure is low and the heart tones are rapid distant and weak

serious in a diabetic It interferes with the metabolism of the body and disrupts the balance that the diabetic patient has maintained by exercise *diet and insulin* Any *infection must be looked upon* as an important matter because it may produce coma in a diabetic

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1 Excessive thirst
2 Vomiting

TABLE I

	Diabetic Coma	*Insulin Reaction*	*Cerebral Accidents*
Onset	Slow	Rapid (few minutes)	Sudden
Food	Excessive	Too little	No influence
Insulin	Little or none	Excessive	None
Infection	Usually	None	None
History	Mild if any	Absent as a rule	Arteriosclerotic or hypertensive after the accident
Pain in the abdomen	Frequent	Absent	May be pain in head
Vomiting	Common	Seldom	After the accident
Fever	Frequent	Absent	May be very high
Skin	Dry	Moist	Indifferent
Appearance	Very sick	Pale and weak	Typical features of hemiplegia
Respiration	Air hunger	Normal	Stertorous
Mental state	Unconscious	Delirious	Usually unconscious or nearly so
Urine	Sugar and diacetic acid	No sugar or diacetic acid but occasionally present on first examination and absent on second	Sugar but no diacetic acid
Blood examination	Hyperglycemia	Hypoglycemia	Normal or slightly elevated
CO_2 combining power	Reduced to 20 volumes per cent or below	Normal	Normal

f The eyeballs are soft due to lowered intraocular tension and are therefore sunken back in the sockets

g Oliguria and then anuria develop

2 The components of the ketosis complex may be enumerated as follows

a The breath has a peculiar fruity odor

b Breathing is deep though not necessarily rapid and is known as the Kussmaul type

c The urine contains large amounts of sugar acetone and diacetic acid

d The blood sugar is elevated though the degree of elevation as such is not an index of the severity of the diabetic coma

e The carbon dioxide combining power of the blood drops down to 20 volumes per cent or lower at times

Diagnosis The differentiation between diabetic coma and other *types of coma is usually easy if the urine is tested for sugar diacetic* acid and acetone When there is any reason for doubt a carbon dioxide combining power determination of the blood should be done this is low in diabetic coma and not ordinarily changed in other kinds

The commonest disorders that are confused with diabetic coma are

1 Hypoglycemic reaction from insulin
2 A cerebral accident in a patient who is also a diabetic
3 An injury to the brain or skull by accident
4 Acute alcoholic coma

If the history relates that the patient has had diabetes and if there is a story of progressive thirst vomiting nausea air hunger and drowsiness the diagnosis is simplified It is always well to remember the rule that the urine should be examined a second time particularly when the clinical picture and the urinalysis do not seem to fit one another This is especially true when the problem of insulin reaction *arises because some sugar may be found in the first urine specimen* which in reality is a mixture of residual sugar-containing urine giving one the false impression of a truly positive urinary sugar

The table on page 145 may be used in the differentiation between diabetic coma insulin reaction and cerebral accident

Prognosis Recent years have shown a marked decrease in the mortality rates due to *diabetic coma attributable no doubt* to a growing realization that diabetic coma is an acute severe emergency demanding immediate action close study and follow up corrective

different methods of determining and administering insulin but the chief point to remember in any form of treatment is that the amount of insulin must be large and the doses repeated every hour or two until acidosis is controlled

After the diagnosis is established an immediate preliminary dose of 100 to 200 units of regular or crystalline insulin should be given subcutaneously Occasionally the intravenous route may be used if absorption is expected to be slow Additional amounts are given at intervals during the first 3 hours and may be calculated according to the patient s clinical status and the blood sugar level The following routine may be applied

Initial Blood Sugar (mg per 100 cc. Blood)	*Additional Units Required*
300 to 600	50 to 100
600 to 1000	200
Over 1000	300

It is desirable to follow the progress of treatment by frequent blood sugar determinations if possible as has been indicated above and also by repeated examinations of the urine for sugar acetone and diacetic acid It will be a simple procedure to examine the urine quite frequently if a catheter is placed in the bladder and left in situ while the patient is unconscious Each time the bladder is drained for a sample all residual urine should be removed and the bladder irrigated with a mild antiseptic solution

In my experience coma has been controlled with 200 to 250 units of insulin in 24 hours although severely unconscious patients may require as much as 500 and even 1000 units in the first 4 to 5 hours Fowler Benson and Rabinowitz have treated patients with 100 units of regular insulin intravenously 100 units of regular insulin and 200 units of protamine zinc insulin intramuscularly They believe these large doses are more effective than intermittent administration of small doses

b Treatment of dehydration

(1) The total body salt of a normal adult is approximately 175 Gm During severe diabetic coma more than 30 Gm of this supply may be lost. Intravenous administration of 1000 cc of normal saline is indicated at once to correct dehydration and loss of base 1000 cc. of saline may be given subcutaneously These fluids must be given slowly and at slightly above body temperature Within the first 24 hours the aim is to give the patient in diabetic coma from 4000 to 6000 cc. of fluid. In the absence of nausea and vomiting fluid may be given by mouth Administration of fluids helps build up the blood volume and starts production of new bases It should also increase the urine output. If the patient has been anuric

procedures Thus within the past decade the mortality rate has decreased as much as 20 per cent It must be remembered however that mortality figures include patients with coma who died as a result of complications other than coma

TREATMENT

Since diabetic coma is an acute medical emergency if it is at all possible the patient should be hospitalized in an institution where 24 hour laboratory service is available The active treatment may be divided into (1) general and (2) specific

1 General
  - *a* Warmth is important External heat is applied by equipping the bed with warm blankets in place of sheets Electric pads hot water bottles and irons are not used because of the danger of causing burns
  - *b* A catheter is inserted and the bladder drained The urine is examined for sugar acetone and diacetic acid A determination of albumin and sediment in the urine may be helpful
  - *c* The patient must have a blood sugar determination done immediately and it is well to ascertain the amount of nonprotein nitrogen and cholesterol in the blood at the same time Probably the most important factor in the blood work is the determination of the carbon dioxide combining power This determination should be made at frequent intervals during the course of treatment because the rise in the plasma carbon dioxide combining power is a direct measure of reduction in acetone bodies and is therefore evidence of adequate insulin action A common pitfall is that of relying upon a level of consciousness alone as an index of progress in treatment
  - *d* Circulatory stimulants as coramine 4 to 6 cc or caffeine 0 4 Gm (6 grains) may be given intramuscularly and repeated every four to six hours if necessary
  - *e* Gastric lavage is done soon after entrance to the hospital If the stomach is emptied the patient will not vomit and the possibility of his aspirating fluid or undigested food into his lungs is ruled out
  - *f* A cleansing enema is of value particularly if abdominal distention is present

2 The specific treatment must be aimed at treating the ketosis with large doses of insulin and administering an abundance of fluids to overcome dehydration Undoubtedly the greatest single factor in the reduction of mortality in coma is the vigorous employment of large doses of insulin during the first 2 to 3 hours of treatment
  - *a* Treatment of ketosis
    - (1) Insulin The amount of insulin given depends on the depth of coma From time to time various authorities have recommended

administration of 1 5 Gm of potassium chloride in the form of a 2 per cent solution in distilled water 2 Gm of potassium citrate may be given orally and the dose may be repeated

(8) As soon as it is convenient the patient who has been brought out of coma is placed on three or four regular feedings a day with an appropriate dose of regular insulin accompanying each feeding until the amount of insulin required to control the diabetes is established.

HYPOGLYCEMIA AND HYPERINSULINISM

The terms hypoglycemia and hyperinsulinism are used interchangeably but they do not denote exactly the same thing Hypoglycemia is most commonly an effect of hyperinsulinism but it may also be produced by other conditions as deficiency of the liver cholera and constitutional disorders as Addison s disease hyperpituitarism and hemochromatosis Hyperinsulinism may be caused by hyperplasia hypertrophy adenoma or carcinoma of the islands of Langerhans

Etiology Organic and functional causes of hypoglycemia are recognized The organic causes include (1) Hyperplasia and tumors both benign and malignant of the islets of Langerhans (2) liver diseases (3) endocrine disorders affecting the pituitary such as Simmond s cachexia Frolich s syndrome and acromegaly (4) hypothyroidism (5) endocrine disorders affecting the suprarenal glands such as Addison s disease and adrenal tumors (6) central nervous system disorders such as cerebral degeneration and head injuries (7) post irradiation of the pancreas and (8) patients following gastrectomy

The functional causes of hypoglycemia are the following (1) Hyperinsulinism due to the administration of excessive amounts of insulin (2) renal glycosuria (3) continuous muscular work or progressive muscular atrophy (4) pregnancy and lactation (5) functional disturbances of the sympathetic nervous system and (6) some instances of peptic ulcer and some of neurasthenia

Spontaneous hypoglycemia has been observed also in pernicious anemia miliary tuberculosis and status thymicolymphaticus It should be emphasized however that the commonest causes of hypoglycemia are organic and functional hyperinsulinism and liver disease

Generally speaking the blood sugar level is the expression of an equilibrium between the rate of glucogenesis by the liver and the rate

and fails to have a diuresis after fluid administration the outlook is bad On the other hand when diuresis occurs following fluid administration the prognosis is very good

(2) Administration of glucose *intravenously or subcutaneously* during diabetic coma is still a controversial issue Injection of 5 or 10 per cent glucose with the appropriate amount of insulin is a common procedure Root believes the overfeeding of coma patients with excessive amounts of glucose (amounts per hour greater than caloric needs) is one of the principal errors and causes of death in coma cases Suggested contraindications to the administration of glucose at least until treatment is successful are the following (a) Danger of pancreatic exhaustion (b) anuria (c) excess of sugar in the body fluids (d) peripheral circulatory failure—best combatted with blood plasma and serum (shock may be an indirect result of early glucose treatment) (e) loss of critically low sodium chloride to subcutaneous glucose depots (f) obscured follow up of blood and urine determinations (g) deficiency of serum potassium with paralysis of voluntary muscles following excessive use of glucose in coma

(3) After a cleansing enema 1000 cc of tap water may be given per rectum by drip method

(4) When the blood and urine sugars show a decided fall and the patient begins to react favorably fluid administration may be reduced and doses of insulin spread farther and farther apart

(5) Considerable difference of opinion continues regarding the use of alkalies in the treatment of coma Relatively few employ sodium bicarbonate solutions on the basis that they produce alkalosis and often edema I prefer to use sixth molar sodium racemic lactate 500 to 1000 cc according to the carbon dioxide combining power level Hartman s formula for determining the amount of lactate solution necessary to raise the carbon dioxide combining power of the blood to normal (60 volumes per cent) is as follows cc of molar sodium lactate = (60 — plasma CO_2 content) × (0 3 × body weight in kilograms)

(6) The use of blood transfusions is of value in some cases and plasma has been used For optimal results it is desirable to use blood and blood derivatives before evidences of shock due to diminished circulating blood volume occur

(7) In some cases of coma a fall of the blood potassium level will occur during the course of treatment The symptoms resulting are weakness respiratory difficulty increased pulse pressure dilatation of the heart and elevated venous pressure The depletion of blood potassium is probably due to loss by diuresis low potassium intake and possibly a shift from extracellular to intracellular space In the low potassium level phase the condition may be corrected by the

diagnosis Obtaining a sample of blood for sugar determination during the acute episode serves to clinch or abjure the diagnosis Sugar tolerance tests are not very reliable but if the blood sugar is below 60 mg per cent during an attack and relief is obtained by the intravenous administration of glucose the patient has hypoglycemia It should be remembered that it is not the level of blood sugar per se but the rapidity with which hypoglycemia has been produced that produces the clinical syndrome Other tests which may be of aid in diagnosis are Dextrose tolerance tests tests of liver function and response to insulin and ephedrine Electrocardiographic tracings may be abnormal before and normal following the administration of glucose during an attack

Mild stages of hypoglycemia may be mistaken for alcoholic intoxication petit mal hysteria psychoses encephalitis or organic brain lesions Severe cases are confused particularly with epilepsy (grand mal) hysteria brain tumor and sometimes with cerebral injury or hemorrhage Before making a final diagnosis of hyperinsulinism other disorders as carcinoma cirrhosis or subacute atrophy of the liver and diseases of the adrenals pituitary and thyroid must be eliminated Infections and poisons also produce hypoglycemia Genuine hyperinsulinism is usually caused by hypertrophy and hyperplasia of the islands of Langerhans and more rarely by carcinoma or adenoma of the islands

In organic types of hypoglycemia symptoms occur typically in the early *morning This fact may frequently help to differentiate the type* of hypoglycemia present

Prognosis Prognosis is usually favorable though it depends on the cause Obviously islet cell carcinoma or diffuse carcinomatosis of the liver carry a much more ominous prognosis than the hypoglycemia reaction for example of severe continuous muscular work The tendency toward obesity in these cases is unfavorable

TREATMENT

1 The treatment of hypoglycemia is dependent on the cause If it is due to an adenoma or carcinoma of the islands surgical exploration should be done and the adenomatous or carcinomatous tissue removed if possible This usually results in a cure If symptoms per

of glucose removal from the blood by the tissues This equilibrium is dependent upon several factors (1) The integrity both functional and organic, of the tissues which contribute and remove glucose from the blood (2) the endocrine system and the central nervous system which together regulate these tissues (3) a chain of enzymes through the action of which glucose is metabolized Thus any functional or disease process which results in a hormonal dysfunction disintegration of hepatic and other body tissues and the body s enzymatic functions may result in spontaneous hypoglycemia and its symptoms

Signs and Symptoms The syndrome of hypoglycemia has become universally recognized The typical picture is seen after an overdose of insulin Clinical features depend upon the severity of the disorder mild moderate and severe forms occur In mild types mental apathy or confusion a change of personality psychic exaltation or depression irritability weakness, insomnia and vague gastrointestinal disturbances may be the only symptoms Usually the pulse rate rises blood pressure may increase pupils dilate and the patient breaks out in cold sweat Hunger is a frequent but by no means constant complaint The patient may also complain of paresthesia notably numbness and tingling in the periphery of the body Headache and restlessness are frequently seen As the disorder becomes aggravated delirium transient loss of consciousness and visual disturbances may occur in addition to the above Later convulsions local or general develop and a state of coma may terminate the clinical course Neurological symptoms and signs may occur alone or in almost any combination Amnesia and aphasia may occasionally become prominent

Diagnosis It is often difficult to recognize hypoglycemia in the mild form but if a patient has lapses of memory short periods of unconsciousness excessive hunger which is relieved by food a desire to sleep and sweats profusely the diagnosis should be suspected It is important to make an early diagnosis particularly in severe cases for the reason that early diagnosis means early treatment and thereby prevention of permanent cerebral damage Having the condition in mind when a patient has a chain of symptoms which are hard to account for after the usual diseases have been considered is half the

However rare the syndrome may be it is always extremely serious This is attested to by the mortality figures which range from 60 to 90 per cent

Etiology The true cause of hyperthyroid crisis is not known any more than is the cause of hyperthyroidism By some it is looked upon as being actually an intrinsic feature of the disease rather than a com plication and is the result of the patient s failure to adjust to the strain imposed by severe thyrotoxicosis The usual explanation of the thyrotoxic storm is the liberation of excess thyroid hormone due to manipulation at surgery This probably is not the complete picture First of all hyperthermia which is a characteristic feature of thyrotoxic crisis is not a common reaction from the experimental injection of thyroxin Secondly the latent period before the action of thyroxin occurs is considerably longer than the period between surgery and postsurgical crisis Thirdly only a moderate increase of serum iodine occurs after thyroidectomy and in mild crisis

Most cases of crisis have several warning signs in common A severe degree of thyrotoxicosis depleted nutritional status and severe complicating disease Thyrotoxic crisis occurs in miniature it is true and this is exemplified by the moderate febrile reactions following thyroidectomy in patients whose basal metabolic rate has not been brought to normal preoperatively Precipitating factors which may act as the trigger mechanisms in the production of thyroid crisis are thyroidectomy pneumonia iodine withdrawal wound sepsis and postoperative complications Crisis due to infections such as pneu monia and upper respiratory infections has been referred to as medical storm and crisis following trauma postoperative or otherwise has been referred to as surgical storm There is actually no real difference between the two

Pathology Autopsies on patients dying in hyperthyroid storm reveal a high incidence of the following chief cardiac pathological findings Coronary arteriosclerosis and hypertensive heart disease alone or in combination and with or without failure Secondly there is a high incidence of pulmonary complications Tracheitis bron chitis bronchopneumonia or pulmonary edema Thirdly pathologic changes in the liver notably central necrosis and fatty degeneration

Signs and Symptoms The symptomatology of hyperthyroid crisis is dependent upon relative vulnerability to the stress of thy

sist there may be multiple tumors or malignant degeneration Often an adenoma is too small to be palpated through the abdomen and as a result the area must be explored at operation

2 Most cases of hypoglycemia are due to other causes which can be remedied by medical treatment

a Drugs as epinephrine ½ to 1 cc of 1 1000 solution hypodermically may be used to stimulate the glycogenic breakdown in the liver and keep the blood sugar at a somewhat raised level Epinephrine in oil acts to elevate the blood sugar without causing undesirable reflex hyperinsulinism

b The most important principle in treatment particularly of functional hypoglycemia is a dietary regimen with frequent feedings five or six a day and the use of a high fat low carbohydrate and relatively high protein diet For the average adult 180 Gm of fat 90 Gm of carbohydrate and 100 Gm of protein may be given The high fat intake slows the emptying time of the stomach and lets the carbohydrate into the system at a slower rate Slowly utilizable carbohydrate is also afforded by the high protein diet Each patient must be considered individually however since obesity may become a problem

c The patient suffering from an acute attack of hypoglycemia should be given 50 to 100 cc of 25 or 50 per cent glucose intravenously If the patient is conscious orange juice with or without sugar dextrose syrup or dry sugar placed in the mouth will be of benefit It is a good practice for these patients to carry lump sugar with them at all times in the event that symptoms arise

d The use of small doses of insulin before meals is frequently attended by excellent results because its administration prevents hyperglycemia and a reactive hyperinsulinism

e Emotional disturbances overexertion exposure to cold and delayed meals are to be avoided since they have a tendency to lower the blood sugar to symptomatic levels

f Possibly the one exception where a high carbohydrate diet with supplemental glucose administration is indicated is in hypoglycemia secondary to diffuse hepatic disease In such a case the treatment of the hypoglycemia will be essentially that of the primary pathological process in the liver

ACUTE HYPERTHYROID CRISIS

Thyrotoxic crisis or acute hyperthyroid crisis is a clinical reaction peculiar to hyperthyroidism It is now seen only rarely in its typical form because of modern methods of diagnosis and treatment It is by no means extinct 36 cases were seen in a review of 2033 thyrotoxic patients at Massachusetts General Hospital during the past 25 years

of hyperthyroidism either as a result of surgery as a result of infection or infrequently spontaneously The basal metabolic rate is usually high and may range from plus 50 to plus 100 The white blood count and differential are usually normal unless crisis occurs following pneumonia or some other infection

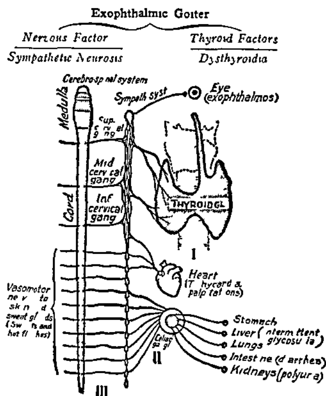


Fig 1 —Symptoms and pathogenesis of Graves Disease

Prognosis While thyrotoxic storm is occurring with decreased frequency it is nevertheless of grave importance whenever it occurs by virtue of its decidedly poor prognosis Depending upon their representative sources the mortality figures of acute storm range from 60 to 90 per cent The usual course is a rapid progression of symptoms exhaustion or cardiovascular collapse and death

The prognosis in regard to the heart in acute thyroid crisis depends on the condition of the heart before the crisis sets in

rotoxicosis of the following systems The central nervous system the cardiovascular system and the hepatorenal system Chiefly the clinical picture of hyperthyroid storm will depend upon which of the above systems breaks down first The most prominent features of the disease are hyperpyrexia tachycardia and nervous hyperirritability with delirium When crisis occurs postoperatively its symptoms will usually be noted within 4 to 16 hours following operation

The patient as seen clinically will usually present one of two general pictures of the disease (1) The activated form in which there are seen restlessness proceeding to delirium tachycardia vomiting diarrhea dehydration red beefy tongue hyperpyrexia erythema vasomotor collapse oliguria and occasionally jaundice (2) the apathetic type which is manifested by muscular hypotonia mental apathy and extreme prostration with only a mild elevation of temperature The apathetic form of crisis admittedly occurs much less frequently than the activated form but by virtue of its symptoms it is more difficult to recognize

Symptoms referable to the cardiovascular system frequently occupy the center of the stage in a case of acute hyperthyroid crisis Cardiac symptoms may come on abruptly take a rapid stormy course and terminate either fatally or in prompt recovery depending to a large extent on the skillfulness manifested in the management of the case The cardiac manifestations of the thyroid crisis are characterized by the following events

1 The heart becomes extremely rapid and the blood pressure usually falls However sometimes the systolic pressure rises and only the diastolic phase decreases

2 Auricular fibrillation may develop or the tachycardia may be of the sinoauricular type

3 The heart may dilate and fail

4 There may be *systolic murmurs over the mitral and aortic* areas

5 Sometimes precordial distress even anginal pain is a feature of this stage of the disease

6 Hepatic enlargement may develop and edema of the ankles appear

Diagnosis The syndrome of thyrotoxic crisis is usually easily recognized when the symptoms enumerated above occur in the course

9 Reduction of a prolonged prothrombin time with vitamin K 20 mg intramuscularly twice daily

10 Correction of cardiac failure In the main the treatment of heart failure is similar to that in other types of failure In the presence of auricular fibrillation digitalis is as effective as in other forms of heart disease However it will rarely affect the tachycardia of hyper thyroidism Quinidine is a good means by which to change auricular fibrillation to normal rhythm postoperatively Otherwise the final treatment of cardiac failure due to hyperthyroidism is the treatment of hyperthyroidism itself When quinidine is used it may be ad ministered in 0 33 Gm (5 grains) every 3 to 4 hours for six or eight doses

Evidences requiring the discontinuance of quinidine therapy are buzzing in the ears and deafness increase in the irregularity of the heart or heart rate nausea vomiting faintness or dizziness If the desired results have not been obtained after 2 66 Gm (40 grains) of quinidine has been administered it is useless to continue the drug

Preoperative Treatment The most important features in pre paring a patient for operation are

1 *Administration of Iodine* Since Plummer first began the routine use of Lugol s solution in preparing a patient for thyroidec tomy this procedure has become a standard routine Lugol s solu tion is given in doses of 0 33 to 0 66 cc (5 to 10 minims) three times a day It is difficult to determine just how long this should be con tinued but about two weeks is the usual time The basal metabolic rate may be used as a guide for the time of operation but the clinical condition of the patient is more important Usually the basal meta bolic rate is reduced to its lowest level in about ten days and opera tion may be done within the next seven or eight days The psychic condition of the patient, the pulse rate respiratory rate and gain in weight are important identification marks of control of the toxicity

2 *Propylthiouracil* Propylthiouracil has almost completely re placed the more vigorous and toxic thiouracil in the preparation of patients for surgery It is particularly useful in iodine fastness and hyperthyroidism with severe complicating cardiac disease It is customary to give iodine in the usual dosage for at least 3 weeks before operation Propylthiouracil is discontinued one week before surgery to prevent excessive vascularity of the gland at surgery The

and on the age and condition of the patient in general In younger people whose hearts were in normal condition before the onset of crisis the chances of complete recovery are very good On the other hand if the individual is older and has suffered from chronic cardiac ailments the additional insult of acute thyroid crisis either before or after operation is often more than the heart can withstand

TREATMENT

Treatment of the Crisis Since the basic pathologic physiology is unknown there is no truly rational approach to the treatment of hyperthyroid storm The important things to remember are early recognition anticipation in certain types of cases and thorough *preparation of patients for surgery The aims in treatment may be* enumerated as follows

1 Prevention of tissue anoxia This is accomplished by the administration of oxygen by suitable means

2 The inhibition of discharge of thyroid hormone from the thyroid gland This is effected by giving 10 drops of Lugol s solution orally three times a day In patients who are vomiting 2 to 4 Gm (30 to 60 grains) of sodium iodide may be administered intravenously during the day After the acute crisis is controlled the dose of Lugol s solution may be decreased to 0 60 to 1 cc (10 to 15 minims) daily

3 Suppression of the manufacture of new thyroid hormone by giving thiouracil or one of the allied preparations

4 Rest for the patient extremely important and obtained by the following Morphine sulfate 0 016 Gm (¼ grain) hypodermically sodium bromide 1 Gm (15 grains) chloral hydrate 1 Gm (15 grains) or sodium amytal 0 2 Gm (3 grains) orally

5 Protection of the liver accomplished by the administration of 2000 to 3000 cc of 5 per cent glucose intravenously at the rate of *5 cc per minute* and the administration of vigorous doses of vitamin B complex intravenously or intramuscularly

6 Correction of electrolyte balance if any If edema occurs sodium chloride intake should be reduced but fluids should not be discontinued

7 Compensation for possible renal exhaustion

8 Elimination of infection with suitable antibiotics and sulfonamides

d Sulfadiazine in full dosage (8 Gm in 24 hours) is recommended by some as a pre and postoperative measure in an effort to avoid in fections which may result in thyroid crisis Sulfonamides it must be remembered have demonstrated goitrogenic properties

6 X ray treatment of the thyroid gland has been recommended by some as a preoperative measure especially in cases of unusual severity If x ray treatment is given a period of several weeks should elapse before operation because of the condition of the tissue about the neck

7 It has been known for a long time that it is dangerous to operate upon a patient who has an upper respiratory infection It is well to emphasize here that no attempt should be made to remove any focus of infection in a patient with hyperthyroidism More than one patient has been seen by the writer one a physician s wife and another a physician who regardless of advice to the contrary had teeth extracted in an attempt to control an active thyroidism The result was death in the dentist s office in one case and death within 12 hours after extraction in the other

Postoperative Treatment 1 If the patient has been adequately prepared and the operation is skillfully done the postoperative man agement is a matter of watching the patient recover One must always be on guard against upper respiratory infection bleeding and an unexpected hyperthyroid crisis

2 The patient is given a highly nutritious diet after the first 24 hours and an adequate fluid intake is essential

3 Tracheitis may cause the patient some discomfort for the first two or three days following operation A compound mixture of aspirin sodium bicarbonate and lemon juice may relieve the soreness

4 Careful attention must be given to the condition of the atmos phere of the sickroom Draughts or dry air are apt to pave the way for an upper respiratory infection which is a disagreeable and dan gerous complication Furthermore anyone with an upper respira tory infection of any kind must be prohibited from the room

5 *Subsequent Follow up* Many physicians belive that after the operation is performed the disease has been completely cured but this is not true The treatment after the first month or two post operatively is quite important The patient must be watched for several important complications

usual cases of exophthalmic goiter may be adequately treated with Lugol s solution in the time honored fashion It must be remembered that there is a danger of obscuring the diagnosis in borderline cases of hyperthyroidism by administering propylthiouracil and similar preparations as well as iodine too radically and too early Propyl thiouracil is more completely discussed on page 160

3 *Diet* The diet should be rich in carbohydrate and 4000 to 5000 Calories a day should be given Not only must the carbohy drate content of the diet be kept at a high level but the quantity of protein too must be elevated because of the demands upon the pro tein stores of the body Vitamins especially B administered orally and parenterally should be employed Hydration must be kept in mind and it is better to keep the intake of fluid at a high level a few weeks before operation than to have to administer large volumes intravenously after operation The risk of the operation is considered less if the patient is well hydrated and has begun to gain weight before thyroidectomy is attempted

4 *Rest* Formerly it was thought best to keep the patients abso lutely quiet for a period of two weeks before the operation However the best results are obtained today by allowing these patients provid ing the heart condition permits to be up and around the home or hospital every day in order to keep the muscle tone of the body at a proper level Patients may be kept in bed for part of the day but absolute bed rest is not a good way to prepare them for operation

We have spent too much time in the past keeping a patient in bed and overlooking the more important psychic outlook of the patient A cheerful attitude should be maintained by all those attend ing a patient being prepared for operation This is true of any operation but it is especially true for a patient who is highly unstrung from a long siege of hyperthyroidism

5 *Other Medications*

a Phenobarbital 0 1 Gm (1½ grains) two or three times a day

b Digitalis in digitalizing dosage may be of value if auricular fibrillation and heart failure are present

c If auricular fibrillation alone exists quinidine 0 33 Gm (5 grains), every four hours is probably better than digitalis

It is best to administer these drugs preoperatively rather than post operatively because of the danger of embolism which may follow the initial doses.

goiter under control and somewhat more than this period is required for the adenomatous type

In addition to a reduction in the basal metabolic rate patients who tolerate propylthiouracil usually show subjective improvement in weight gain and a decrease in pulse rate and blood pressure An abatement of tremor sweating and palpitation also may be noted However the size of the gland is seldom decreased and at operation the gland may be very vascular and friable if propylthiouracil is not discontinued a week or 10 days prior to surgery Also the administration of iodine before operation helps to eliminate this undesirable side effect

Factors which should make one wary of the use of thiourea preparations are these Previous histories of multiple allergies previous history of reaction to one of the thiouracil preparations sulfonamide sensitivity severe exophthalmos preexisting blood dyscrasias toxic adenomata adolescence preexisting hepatorenal disease and pregnancy The indications for the drug are now quite well founded Instances such as poor operative risks (cardiac patients and individuals with advanced hyperthyroidism and cachexia) recurrent hyperthyroidism iodine fastness and iodine hypersensitivity hyperthyroidism recurring after previous surgery and patients with hyperthyroidism upon whom surgery cannot be performed for any reason

It is still too early to make any forecast of the permanence of remissions from hyperthyroidism following withdrawal of the drug Experience has shown that in very few cases has it been possible to discontinue propylthiouracil without recurrence of hyperthyroidism thereafter

a Hypothyroidism may gradually set in any time from a few months to a few years after thyroidectomy Frequently this insidious hypothyroidism is not recognized until a glaring myxedema develops This can be controlled of course by a few grains of thyroid substance every day

b Following operation a patient may develop evidences of hypoparathyroidism which results from injury to the parathyroids at the time of operation *This may be controlled by calcium parathyroid* substance or dihydrotachysterol

c If the patient has had a long standing hyperthyroidism before operation the danger of chronic heart disease must be kept in mind and it is wise to make careful examination of the cardiovascular system at frequent intervals for at least a few years after operation

Propylthiouracil As we have indicated before propylthiouracil has almost completely replaced thiouracil in the treatment of hyperthyroidism Admittedly thiouracil is a more vigorously acting drug and the response to its use is more rapid However the incidence of untoward reactions such as agranulocytic angina leukopenia dermatitis severe anemia jaundice and purpura has caused this drug to be omitted almost completely

The site and mechanism of action of propylthiouracil is not completely understood However its actions are probably in the nature of the following (1) Prevention of the synthesis of thyroxin (2) blockage of the conversion of iodides to iodine (3) lowering of the basal metabolic rate With thyroxin propylthiouracil *has no effect* neither has it any evident effect on the thyrotropic hormone as a matter of fact it may even stimulate its formation The exact mechanisms by which propylthiouracil and similar drugs inhibit the formation of thyroid hormone are unknown but evidently it is accomplished by the inhibition of enzyme systems which are concerned with the formation of thyroid protein or with the combination of thyroid protein with iodine

A dosage of 300 mg daily until relatively basal levels are obtained is usually adequate Such patients then may be maintained on 75 mg daily While propylthiouracil is less toxic than thiouracil its action is slow and it takes roughly one and one half times as long to produce similar results On a dosage such as that listed the basal metabolic rate may come down at the rate of about 1 per cent daily Normally about 10 to 12 weeks is required to bring a patient with diffuse toxic

Erb s sign is based on the fact that in tetany muscular response occurs with galvanic current of weaker strength than normal Chvostek s sign is dependent upon the mechanical stimulation of the facial nerve by tapping the skin just anterior to the external auditory meatus Twitching of the facial muscles indicates a positive reaction Trousseau s phenomenon is noted when the arm is compressed circu larly above the elbow with a resultant typical contraction of the muscles of the hand to form the so called obstetrical position

The first evidences of active tetany are carpopedal spasm con vulsions and laryngeal spasm These muscular contractions occur spontaneously and are usually preceded by a tingling sensation slight numbness stiffness and difficulty in moving the extremities The wrist and elbow are flexed the hand stiff and arched and the fingers rigid with the thumb covered by the fingers which are usually bent only at the metacarpophalangeal joints When the lower ex tremities are affected the heel is pulled up the sole arched and the leg extended Spasm of the diaphragm when it occurs may cause death due to inspiratory or expiratory apnea Involvement of the glottis is recognized from the noisy and difficult breathing It occurs upon very minimal stimulation and is most frequently seen in chil dren Convulsions are usually generalized but may occur unilaterally or in muscle groups In severe tetany convulsions may result in death particularly if the seizures are prolonged or occur frequently

Spasm may occur as a result of involvement of autonomic nerves and smooth muscle and is seen in the gastrointestinal tract the iris the bronchi the heart and the urinary bladder Similarly angio spasm may occur and result in edema pallor dermographia and pain in the extremities

Mental symptoms when they occur usually take the form of irritability confusion hallucinations restlessness and apprehension Occasionally psychiatric disturbances bordering on hysteria or out right psychoses may develop In cases of long standing tetany lens opacities are of common occurrence calcification of brain tissue occurs occasionally and degenerative changes of the nails hair and teeth are not at all unusual

Diagnosis As a rule the diagnosis of tetany is made with ease and is based upon the history and clinical picture However the im portant problem is the determination of the underlying complaint

CHAPTER IX

Metabolic Disorders

(Continued)

TETANY

Tetany is a systemic disturbance rather than a disease itself It has been defined as a syndrome in which there is an abnormally increased reaction of the nervous system to stimuli with resultant painful tonic muscle spasms of muscle groups or in some instances the *entire musculature of the body*

Etiology One or more of the following phenomena are usually associated when tetany appears (1) Hypocalcemia in which there is a decrease in both the ionized and nondiffusable fractions of the calcium (2) hyperphosphatemia and (3) alkalosis Of these the most important are hypocalcemia and alkalosis The causes of hypocalcemia may be enumerated as follows

a Hypoparathyroidism is the most common cause in this group It is most often noted about 24 hours after radical thyroid operation and it may last for days or years

b Rickets or osteomalacia inadequate calcium intake steatorrhea administration of alkaline phosphates excessive excretion of calcium and renal insufficiency with phosphorus retention also cause or lead to tetany

The causes of alkalosis are

a Hyperventilation usually due to an emotional disturbance most often causes alkalosis resulting in tetany

b Alkalosis may also ensue from ingestion of large amounts of alkali persistent vomiting causing excessive loss of gastric contents etc

Signs and Symptoms Clinically one may distinguish between two stages of tetany latent and active The latent form is characterized by neuromuscular excitability it is true but no frank symptoms are presented These however may be elicited by proper stimulation of peripheral nerves In the active form there is tonic spasm of various muscle groups as well as convulsions in some instances

Latent tetany may be demonstrated by several specific reactions Of these Erb s Chvostek s and Trousseau s signs are most helpful

the tetany which occurs in steatorrhea and similar sprue syndromes is the administration of vitamin D and calcium salts and the correction of the underlying impairment of intestinal absorption of fats Treatment of tetany due to hypoparathyroidism and alkalosis will be discussed in detail in subsequent sections

HYPOPARATHYROID CRISIS

Hypoparathyroidism is a specific deficiency disease due to complete or relative absence of parathyroid hormone and manifested by the phenomena of tetany and certain specific alterations of blood chemistry It occurs in both primary and secondary forms

Etiology Primary hypoparathyroidism may be due to fibrosis primary atrophy or cystic degeneration of the parathyroid glands Secondary hypoparathyroidism occurs as the result of the accidental removal of the parathyroid bodies during thyroidectomy and the intentional removal during parathyroidectomy The outstanding metabolic features are (1) Fall in the blood calcium (2) normal or elevated serum phosphorus concentration (3) decrease of calcium in the urine (4) normal acid base balance (5) normal serum phosphorus and (6) absence of skeletal defect

Signs and Symptoms The increase in neuromuscular excitability known as tetany is the outstanding symptom of hypoparathyroid crisis This evidence together with restlessness mental irritability and depression forms the main clinical evidences of parathyroid deficiency Manifestations usually appear within a few hours to a few days after surgery but instances are on record in which an interval of several weeks elapsed Details of tetany both latent and active have been previously described

Diagnosis The characteristic contractures of the hands so-called obstetric position phalanges flexed with the middle and the distal contracted down into the palm of the hand present a typical picture These and similar features together with proper studies of the blood and urine usually clinch the diagnosis The significant chemical findings are a low serum calcium which may be as low as 5 mg per 100 cc a high serum phosphorus which may rise to 12 mg per 100 cc absence of calcium in the urine and normal serum phosphatase activity The heart rate may be considerably increased and the elec

The important laboratory studies to be made are the serum calcium the serum carbon dioxide combining power serum chlorides the *p*H of the urine and the concentration of calcium in the urine

The important chemical findings of tetany when due to hypoparathyroidism are a low serum calcium (7 5 mg per 100 cc or less) high serum phosphorus (up to 11 or 12 mg per 100 cc), a prolonged clot retraction time and absence of calcium in the urine Electrocardiographic tracings reveal the R T interval to be prolonged to 0 30 to 0 35 second When tetany is due to alkalosis brought on by hyperventilation the carbon dioxide combining power of the serum may *be slightly reduced Calcium is present in the urine in normal* amounts as determined by the Sulkowitch test The urine characteristically is alkaline In tetany due to the ingestion of large amounts of alkali one encounters an alkaline urine normal concentration of calcium in the urine and a high carbon dioxide combining power in the serum If the tetany is due to alkalosis as a result of loss of gastric contents the urinary and blood findings are similar but in addition there is a marked lowering of the serum chlorides

Conditions which may simulate tetany and which occasionally *will cause difficulty as far as differential diagnosis is concerned* are uremia tetanus meningitis and certain type of intoxications i e lead strychnine and atropine

Prognosis The prognosis of tetany is actually that of the underlying disease The outlook has become more cheerful with the advent of newer methods of treatment When the cause is discovered and eliminated and the proper acid producing salt administered tetany usually disappears Tetany due to alkalosis and chronic tetany offer excellent prognoses

TREATMENT

Obviously again the treatment of tetany is that of the disease process which underlies it In general treatment of this syndrome is concerned with the correction of various aspects of abnormal blood chemistry notably hypocalcemia hyperphosphatemia phosphate retention parathyroid deficiency and increase in the alkali reserve Infantile tetany maternal tetany and the tetany of osteomalacia are dependent upon vitamin D deficiency and an inadequate calcium intake Accordingly the remedy is vitamin D supplements and the additional intake of adequate amounts of calcium The treatment of

cium gluconate, 10 cc of 20 per cent solution may be administered intramuscularly

Limitation of Phosphorus The intake of phosphorus in the diet should be strictly limited Foods to be avoided to maintain a low phosphorus level include meat eggs milk and milk products wheat cereals potatoes and legumes While milk has a high calcium content it also contains a high percentage of phosphorus and therefore should not be employed in the treatment of hyperparathyroidism

Parathyroid Hormone Parathyroid hormone is most effective in acute tetany and reduces the need for repeated injections of calcium salts Dosage depends upon the degree of hypocalcemia and the severity of the disease The usual dose is 1 to 3 cc (100 to 300 units) injected subcutaneously It may be necessary to repeat injections every 8 to 18 hours Excessive doses are to be avoided and prolonged usage is unwise due to the possible development of refractoriness to the hormone and because of the dangers of toxic effects due to over dosage

Dihydrotachysterol (AT 10) Dihydrotachysterol is similar to vitamin D in its origin and in its action It facilitates the absorption of calcium from the intestinal tract and increases the excretion of phosphate in the urine It does not appear to have any antirachitic effect Overdosage results in hypercalcemia manifested by nausea vomiting diarrhea headache abdominal cramps fatigue and polyuria which may go on to dehydration coma and death This potent drug while admittedly dangerous unless carefully controlled has largely supplanted parathyroid hormone in the treatment of parathyroid deficiency The dosage varies with the degree of hypocalcemia and the response of the patient Between 3 to 10 mg (1 25 mg /cc in oil) daily for several days is usually necessary until the serum calcium rises to the lower levels of normal The drug should be administered with caution because the complete effect upon serum calcium is not noted for 48 hours Hereafter 1 to 3 mg a day may be adequate It should be emphasized that the drug must be carefully controlled to avoid hypercalcemia skeletal decalcification and metastatic calcification This is accomplished by frequent determinations of the serum calcium and by employment of the Sulkowitch test for calcium in the urine

trocardiogram is characteristic in many cases It is featured by an abnormally prolonged S T interval

The diagnosis of tetany in its latent form may be made by

1 Demonstration of hyperirritability by testing for Chvostek s or Trousseau s sign

2 Demonstration of electrical hyperirritability by electrical stimuli (Erb s phenomenon)

3 The usual chemical changes in the blood

4 Prolongation of S T interval on the electrocardiogram

Hysteria is one condition which is apt to give great difficulty in differential diagnosis However remembrance of the fact that the calcium and phosphorus metabolism is disturbed nearly always leads *to the proper diagnosis*

The tetany of alkalosis is almost completely identical to that of hypoparathyroidism The differential diagnosis is made on the basis of history and corroborative laboratory evidence

Prognosis Patients with acute hypoparathyroidism may die in a state of exhaustion unless the proper measures of treatment are instituted Chronic hypoparathyroidism is often compatible with life for many years Most patients especially younger individuals may be maintained in good health for many years by simple therapeutic measures and as a rule the tetanic convulsions are not so fatal as they are terrifying

TREATMENT

The objective of treatment is the correction of the existing disorders Hypocalcemia hyperphosphatemia and parathyroid deficiency This is accomplished by the administration of calcium the reduction in the intake of phosphorus and substitution therapy

Calcium Administration (1) For the emergency treatment of acute tetany 10 cc of 20 per cent calcium gluconate or 10 to 20 cc of 5 per cent calcium chloride intravenously usually brings immediate relief It may be necessary to repeat this procedure two or three times a day and the injection should be given slowly to avoid reactions (2) For the treatment of chronic tetany or for the establishment of a maintainance dose large doses of calcium lactate approximately 2 Gm (30 grains) should be dissolved in water or fruit juices and administered orally every 4 hours (3) In some instances cal

Signs and Symptoms In general the signs and symptoms of alkalosis are those of the underlying disease plus those of tetany when it develops Mild grades of alkalosis seldom produce symptoms Increase in the severity of the condition causes restlessness increased irritability and excitability There is decreased pulmonary ventilation at first in volume and then in rate until respirations may be reduced to five to ten per minute This decreased respiratory function leads to an elevation of carbon dioxide percentage in the alveolar air but at the same time there is a reduction in the oxygen partial pressure and in extreme instances cyanosis will result The respirations as a rule are deep in the alkalosis of primary hyperventilation and are shallow in the alkalosis of alkali excess The symptoms of neuromuscular excitability are identical with those due to loss of calcium and are corroborated by the typical signs of tetany Erb s Chvostek s and Trousseau s phenomena and the typical muscular contractions There is however no evidence that the effect is exerted through calcium indirectly Alkalosis due to loss of acids is commonly accompanied by marked dehydration with the symptoms thereof

Diagnosis The diagnosis is suggested by the clinical picture and is corroborated by the following laboratory aids In alkali excess typically the carbon dioxide combining power is high serum chlorides are lowered the *p*H of the blood is increased the serum calcium is normal and the urine is alkaline in alkalosis due to carbon dioxide deficiency through hyperventilation the serum calcium is normal the plasma bicarbonate is reduced the *p*H of the blood is increased and the urine alkaline In some instances the clinical picture may closely resemble that of acidosis or renal insufficiency

Prognosis The prognosis of alkalosis due to most types of hyperventilation is favorable whereas it tends to be guarded in instances of alkali excess due to organic disease processes The usual prognostic implications of whatever pathological process underlies alkalosis must of course be observed

TREATMENT

Correction of the disturbed acid base balance and of dehydration when present is necessary Treatment will vary with the underlying condition producing the alkalosis

Other Medications Vitamin D, while recommended as a means to promote calcium absorption from the intestines may cause an increase in the serum phosphorus and an aggravation of the tetany The common sedatives such as chloral hydrate and barbiturates are sometimes helpful in the treatment of severe convulsive seizures Ammonium chloride in doses of 3 3 Gm (50 grains) three times a day liberates calcium from the stores in the body and helps control the tetany

ALKALOSIS

Alkalosis is a clinical condition in which the bicarbonate of the blood rises above the normal level or in which there is an excessive loss of acid from the body without compensatory loss of alkali

Etiology Carbon dioxide may be lost from the blood by hyperventilation and this phenomenon is observed clinically in the following conditions Fever hysteria high external temperatures second stage of anesthesia the hyperpnea occurring at high altitudes *and encephalitis with respiratory center disturbances and hyperventilation*

Alkali excess occurs by increased formation in the body or by oversupply and is met with in the following conditions (1) Loss of the acid chlorine radical in excessive amounts as in prolonged vomiting or uncompensated gastric lavage causing the sodium *thus released* to combine with the carbon dioxide and thereby to increase the bicarbonate in the blood This is in effect the replacement of a neutral salt sodium chloride by alkaline sodium bicarbonate (2) Excessive administration of alkaline substances as in the treatment of peptic ulcer and occasionally in the treatment of acidosis in chronic *renal* disease (3) The alkalosis resulting from x ray and radium therapy (4) So-called congenital alkalosis possibly due to the disturbances of the carbonic anhydrase

In any event compensatory mechanisms normally take place Decreased formation of ammonia by the kidney retention of *acid* metabolites decreased acid excretion in the urine increased alkali excretion in the urine and decreased pulmonary ventilation When these mechanisms are no longer able to compensate for the abnormal conditions previously cited the clinical condition of alkalosis occurs

halation Other acids such as sulfuric phosphoric and lactic acids may be eliminated through the kidneys Accordingly carbon dioxide may accumulate in the body in any condition which interferes with normal expiration Such conditions are those of narcosis with diminished pulmonary ventilation pulmonary emphysema many cases of cardiac decompensation asthma certain cases of pneumonia bronchitis and pulmonary fibrosis Similarly carbon dioxide may accumulate in the body through rebreathing atmospheres with a high carbon dioxide content When such conditions exist normally and within certain limits compensatory mechanisms take place to effect so-called compensated acidosis These mechanisms are Increase in the rate and depth of respiration increase in ammonia formation by the kidney increase in the acidity of the urine and increase in the alkali reserve of the blood These compensatory mechanisms are so effective as a rule that acidosis due to carbon dioxide excess rarely exists clinically

Of considerably greater importance is acidosis due to alkali deficiency When the removal of base occurs through the intake or production of acid in excess of the regulatory mechanism acidosis follows Outstanding in this group are the following conditions Diabetes mellitus renal failure starvation excessive exercise anesthesia anoxemia dehydration toxemias of pregnancy and the ingestion of acids

In diabetes there is an excessive production of betahydroxybutyric and acetoacetic acids due to faulty fat and carbohydrate metabolism This phenomenon together with the polyuria associated with excessive outpouring of glucose in the urine produces dehydration and marked loss of electrolytes chiefly sodium potassium and chloride The ultimate result is depletion of the fixed base of the body and the production of acidosis Acidosis in diabetes mellitus is discussed in further detail elsewhere

The acidosis of renal failure is associated with an accumulation of the normal acid radicals of the body due to impaired renal elimination In addition there is a loss of the kidney s ability to produce ammonia and in many instances there is a loss of base due to the vomiting of uremia In any event the base of the body is fixed or neutralized by the excessive retention of the aforementioned acids and again the result is acidosis

Hyperventilation Alkalosis

1 Search for and remedy the cause as reassurance and sedation in hysteria

2 *Inhalation* of carbon dioxide which may be effected by breathing 5 per cent carbon dioxide oxygen mixture or by rebreathing carbon dioxide through the use of the paper bag

Alkali Excess

1 *Discontinuation of alkaline therapy*

2 Forcing fluids by mouth will facilitate the excretion of the excess alkali in the blood Ammonium or calcium chloride in doses of 1 Gm (15 grains), three times a day, may be given by mouth and weak hydrochloric acid 0 66 cc (10 minims) in a glass of water may be given three times a day

3 Dehydration and loss of chlorides by vomiting may be corrected by the intravenous injection of 1000 cc of one per cent sodium chloride solution repeated every three hours as long as necessary

4 If the condition has reached the stage of tetany calcium gluconate 10 cc of 20 per cent solution may be given intramuscularly or intravenously for immediate relief or 500 to 1000 cc of one per cent saline solution repeated within an hour if necessary will usually control the situation

ACIDOSIS

Acidosis is an abnormal state of metabolism in which acids are formed or accumulate in the body more rapidly *than they are removed* or neutralized This preponderance of acids in the body may also be effected by the loss of excessive quantities of base A state of acidosis then exists when the hydrogen ion concentration of the blood is elevated above normal (*p*H below 7 3) or when the alkali reserve has fallen below the normal limits

Etiology Under usual conditions of activity and food intake the acid waste products of metabolism exceed the basic The normal excretion of acids is effected chiefly through the lungs and kidneys In the event of failure of either of these two mechanisms an inability of the body to compensate occurs and acidosis is the result Normally the body maintains a strict neutrality at *p*H 7 38 and it is able to maintain such neutrality by the proper excretion of acids largely H_2CO_3 which as a volatile substance can be easily *eliminated by ex*

Diagnosis The following points must be taken into consideration (1) The symptoms of the basic etiological condition (2) the symptomatology associated with acidosis itself and dehydration and (3) corroborative laboratory evidence

The simplest determination of the presence of acidosis is the examination of the urine for the presence of acetone and diacetic acid The test for acetone may easily be performed by putting 5 to 10 cc of urine in a test tube adding a few drops of strong sodium nitroprusside and glacial acetic acid then overlaying the solution with ammonia water If acetone is present a purple color in direct proportion to the amount of acetone in the urine appears between the two layers The test for diacetic acid is made by putting 5 to 10 cc of urine in a test tube and then adding a ten per cent or stronger solution of ferric chloride slowly At first a white precipitate of phosphates is formed more ferric chloride should be added until this dissolves when the resultant color may be noted The presence of a burgundy or mahogany red color indicates the presence of diacetic acid The intensity of the color is of some value in indicating the amount of acid present

The most reliable test is the determination of the carbon dioxide combining power of the plasma according to the method of Van Slyke The normal range is from 45 to 60 volumes per cent The range between 30 and 40 volumes per cent is important because it represents the stage immediately before clinical symptoms appear and is the period when wise therapy may prevent a more serious condition Coma usually supervenes when the Van Slyke index is between 10 and 20 volumes per cent A level of 10 is critical Additional determinations which should be carried out according to the indication are blood nonprotein nitrogen blood urea nitrogen blood chlorides and the determination of urinary ammonia

Prognosis Acidosis is an abnormal physiological state which may appear in a variety of pathological conditions and is not a disease entity in itself The prognosis depends principally on the underlying cause *It should be guarded in any case with clinical manifestations* The prognosis becomes especially poor if the urinary output is decreased or if anuria develops

TREATMENT

Treatment of acidosis in any event is that of (1) Support (2) restoration of fluids (3) restoration of electrolytes and (4) remedy

The acidosis of starvation and fasting is almost identical with that of diabetes and is due to inadequate supplies of carbohydrate with corresponding impairment of fat metabolism

In excessive exercise there is overproduction and incomplete oxidation of lactic acid with accumulation in the blood

It is well known that the alkali reserve is diminished during anesthesia particularly during ether and chloroform anesthesia possibly due to overproduction and retention of lactic acid Lactic acid may accumulate in the presence of anoxemia and impaired carbohydrate metabolism In anesthesia both acetoacetic and lactic acids may appear in the urine

Significant losses of fluids from the body are usually attended by corresponding loss of electrolytes Acidosis may occur particularly when large quantities of base are lost in this manner Removal of base through severe diarrhea may cause acidosis particularly in children and the syndrome is not unusual in diseases of which the chief manifestation is diarrhea for example Asiatic cholera

In the toxemias of pregnancy the same disturbances of the acid base balance which are seen in any instance of prolonged and severe vomiting may occur Acidosis however is much more common than alkalosis

Wherever possible the body attempts to maintain its neutrality through the usual mechanisms of increased ammonia formation by the kidney increased ventilation in which the carbon dioxide is washed out of the blood and increased excretion of acid in the urine Regardless of the causes of acid accumulation when these compensatory mechanisms break down clinical acidosis is seen

Signs and Symptoms Mild degrees of acidosis are not usually recognizable although they may be diagnosed by estimation of the serum or plasma bicarbonate The symptoms of marked acidosis are headache weakness drowsiness abdominal pain tachycardia hyperpnea and occasionally nausea vomiting and pain in the extremities Eventually the respirations become weak stupor and coma follow and death may ensue A characteristic fruity odor appears on the breath due to the excessive production of ketone acids In addition to the foregoing manifestations it must be remembered that the symptoms in any one instance of acidosis are those of the condition underlying the disordered acid base metabolism plus those of acidosis and dehydration

by pigmentation asthenia hypotension gastrointestinal and central nervous system symptoms and aberration of electrolyte and water balance In the long course of the average case of Addison s disease episodes of acute adrenal insufficiency develop at times with explosive suddenness the reason for these remains a mystery During the period of remission the degree of adrenal insufficiency is variable As this chapter is concerned with the acute crisis of Addison s disease the discussion will be limited largely to those aspects of Addison s disease produced by acute adrenal insufficiency

Etiology and Pathology The basic element in the etiology of Addison s disease is an underlying pathologic process of the adrenal cortex present in almost every instance The lesions of the adrenals associated with Addison s disease are tuberculosis atrophy tumors amyloid disease fatty degeneration infections pressure atrophy and vascular lesions including both thrombosis and embolism Of these conditions tuberculosis and atrophy are by far the most important Tuberculosis itself is involved in 50 to 70 per cent of recorded cases of Addison s disease

The essential features of the disturbed physiology in Addison s disease are (1) Increased elimination of salt in the urine associated with decreased concentration of sodium and chlorine in the blood serum (2) inability to concentrate urine under conditions of water restriction and to dilute urine under water plethora (3) increased concentration of potassium in the serum (4) decrease in the plasma volume with corresponding diminution in blood flow (5) fall in blood pressure due to disturbances of salt and water metabolism and decreased blood flow (6) increase in nonprotein nitrogen possibly associated with hemoconcentration and decrease in renal blood flow (7) disturbances in carbohydrate metabolism with significant lowering of the blood sugar level (8) adynamia and languor possibly as a result of salt depletion decreased blood flow and impaired carbohydrate metabolism (9) circulatory collapse and death as observed in acute adrenal crisis and (10) pigmentation of the skin particularly exposed surfaces areas of friction points of pressure and scars

Although the exact cause of the acute adrenal insufficiency is not known many factors may help to precipitate the acute phase Such things as physical exhaustion and fatigue infections (particularly upper respiratory infections) psychic or physical trauma even dietary

of the basic underlying pathology The treatment may be outlined as follows

1 The patient should be kept warm with blankets or hot water bottles

2 Circulatory stimulants such as coramine 4 to 6 cc may be given intravenously and repeated every 2 to 4 hours

3 Gastric lavage usually is unnecessary but may be of considerable value in instances of persistent vomiting

4 Intravenous or subcutaneous administration of 1000 cc of normal saline should be given as soon as possible and may be repeated as often as necessary to raise the blood pressure eliminate evidences of dehydration and elevate the carbon dioxide combining power

5 Alkali may be given in the form of sodium lactate 200 to 1000 cc of sixth molar solution

6 Blood transfusions have been recommended for states of acidosis when there is no diuresis within the first three hours following the first infusion of fluids when the blood pressure remains low or when there is inadequate absorption of subcutaneous fluid in a severely dehydrated individual

7 Upon adequate restoration of electrolyte balance as evidenced by clinical improvement and return to normal of carbon dioxide combining power and blood chlorides 5 and 10 per cent glucose solutions may be given 500 to 1000 cc It is unwise to give glucose solutions subcutaneously as such a procedure may precipitate an acute salt deficiency in an individual whose electrolyte balance is already under grave strain

8 If acidosis is due to uncontrolled diabetes suitable measures must be employed to replace inadequate insulin This subject has been discussed in detail elsewhere

9 The status of the patient as regards his acid base balance and the effectiveness of his peripheral circulation must be investigated repeatedly during therapy through close clinical scrutiny and the suitable laboratory procedures

ADDISON S CRISIS

Addison s disease is a systemic disorder of metabolism due to a chronic pathologic process of the adrenal cortex and is characterized

a The blood sugar is apt to be abnormally low
b The blood nonprotein nitrogen is usually abnormally high
c The blood sodium chloride usually is below the normal of 420 mg per 100 cc and may be as low as 300 mg per 100 cc.
d There is a decided elevation of the blood potassium
e Hemoconcentration as evidenced by a high hematocrit reading may be present
f There may be an increased plasma protein concentration
g Oliguria or anuria with a low specific gravity may be present

5 X ray evidence of calcific deposits in the regions of the adrenals

Obviously the salt restriction test should never be used in suspected cases of adrenal crisis however the water excretion test may be employed in doubtful cases This test is based on the inability of individuals with Addison s disease to make quick excretory adjustment to changes in the intake of sodium and water

Prognosis With newer forms of treatment the prognosis of Addison s disease in general has become considerably more optimistic A great percentage of afflicted persons have been able to resume relatively normal courses of living and activity Untreated patients are unduly subjected to stresses of all kinds and may die as a result of intercurrent infection the advance of the original disease process in the adrenals and throughout the body and the initiation of acute adrenal insufficiency At the present time the majority of individuals having Addison s crisis may be saved if prompt energetic and adequate therapeutic measures are carried out

TREATMENT

Unless adequate treatment is instituted promptly the patient may die The basic principles consist of the correction of the physiologic disturbances i e salt low potassium intake administration of glucose and similar measures and secondly replacement therapy by means of adrenalin adrenal cortical extract and desoxycorticosterone The treatment may be outlined as follows

1 General methods
a Absolute bed rest and warmth with avoidance of all psychic stimulation and aggravation
b Physiological saline with 5 to 10 per cent glucose 3000 to 4000 cc intravenously during the first 24 hours

indiscretions and hot weather have been known to set off acute critical phases The crisis is not apparently dependent upon any marked change in the pathological lesion in the adrenal gland When the critical phase has passed and remission sets in the clinical features which prevailed before the crisis are reestablished Acute adrenal insufficiency may occur without Addison s disease For example in instances of marked adrenal hemorrhage secondary to severe infections (the Waterhouse Friderichsen syndrome) the symptoms and treatment of this type of adrenal insufficiency are identical with those of Addison s crisis

Signs and Symptoms The clinical features of acute adrenal insufficiency (crisis) may vary as to the mode of onset and progression of the disease The onset is usually abrupt but it may be insidious It may follow trauma or infection of any kind or it may come on independently Abdominal pain may usher in the episode or vomiting headache and lassitude may be the initial symptoms Convulsions followed by coma may occur The blood pressure which is usually low in Addison s disease drops still lower and there is peripheral vascular collapse The appearance of the patient is important in the diagnosis There is a grayish pallor and the skin is cold and clammy The pulse is feeble or the patient may be pulseless and the temperature may be subnormal The lassitude and weakness are so pronounced that the examining physician can see in a moment the patient s state of extreme helplessness

Differential Diagnosis This clinical picture may be produced by other diseases associated with shock and confusion in the diagnosis may occur unless certain fundamentals in the differential diagnosis are kept in mind

1 The knowledge that the patient had Addison s disease naturally would be of diagnostic importance

2 A generalized bronzing of the skin with excessive pigmentation in the armpits and groin associated with areas of deep pigmentation on the buccal membrane is significant Observations of crops of black pigmented freckles may make one think of Addison s disease

3 A remarkably low blood pressure as low as 80 mm of mercury or less may be noted

4 Evidences of the typical physiologic disturbances as manifested by the following laboratory procedures

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dramatic improvement on the part of the patient with a return toward normal of the altered features of the metabolism gain in weight and elevation of the blood pressure During the early phases of the crisis it may be impossible to administer medications food or fluid orally In these instances the intravenous subcutaneous intramuscular routes and occasionally the rectum must be employed for the ad ministration of the specific elements in treatment Lastly attention must be given to the avoidance of those conditions known to aggra vate Addison s disease

CAISSON DISEASE

Caisson disease sometimes referred to as the bends compressed air sickness or decompression sickness is caused by an aberration in the exchange and release of inert gases dissolved in the body The phenomenon occurs when an individual is suddenly subjected to rapid reduction in atmospheric pressure after breathing air or other gas combinations under greater than normal pressure With the increase in the use of compressed air for deep water diving and in pier and tunnel construction the appearance of this disease has be come more frequent

Etiology When an individual works under and breathes an at mosphere under greater than normal pressure the various gases in the combination breathed are dissolved in the body according to their solubility in the various tissues The ability of an individual to ac commodate to variations in pressure is determined by his specific manner of inert gas exchange Inasmuch as air is most commonly used in compression work the gases involved are chiefly nitrogen and oxygen Nitrogen as an inert gas is not utilized by the body as is oxygen which is chemically active and readily metabolized The body solvents for inert gases are fats and fluids With a sudden change of greater than atmospheric pressure to normal pressure the dissolved nitrogen gas in the blood the body tissues and fat depots is released with the production of bubbles which result in blocking of the circu lation and tearing of the tissues Nitrogen is approximately six times as soluble in fats as it is in fluids Thus fat depots act as a gaseous reservoir which predispose to bubble formation and it may be con cluded that obese individuals are dangerous risks in compression work of any type Other secondary conditions such as age systemic dis

c Avoidance of purgation

d Search for an elimination of infections by suitable means

e Oral intake of sodium chloride 15 to 20 Gm (225 to 300 grains) in a liter of chilled water daily as soon as the patient is able to tolerate food and medications orally

f Frequent small feedings of sweetened fruit juices or dextrose preparations

g Low potassium high carbohydrate diet Foods high in potassium such as potatoes fish meats soups broths bran condiments dried fruits molasses and chocolate should be limited

h Because of the restricted nature of a low potassium diet administration of ferrous iron 0 6 to 1 Gm (10 to 15 grains) two or three times a day with vitamins A B C D and K should be admini tered

2 Specific methods

a Adrenalin 0 5 to 1 cc in 1 1000 solution may be administered immediately as an emergency measure when the patient is first seen

b Adrenal cortical extract injected intravenously at once in amounts ranging from 20 to 100 cc and administered every 2 or 3 hours or as frequently as needed until clinical response is effected Gradually the amount of adrenal cortical extract may be reduced and a maintainance dosage ranging from 5 to 10 cc daily or every second or third day may be determined

c Desoxycorticosterone 20 to 35 mg in oil injected intramuscularly The maintainance dosage of desoxycorticosterone can only be determined by the study of the individual s salt metabolism and his response to therapy When adequate maintainance dosage of this substance is determined the decision for implantation of desoxycorticosterone pellets may be made One pellet 125 mg is implanted for each 0 4 to 0 5 mg required in the daily dosage Then pellets of the drug are implanted subcutaneously to meet the patient s estimated need for from 6 months to 1 year At the end of this time the patient s hormone requirements are redetermined When subcutaneous implantation is done the hormone is given to the tissues at a slow even rate for a sustained therapeutic effect Other advantages of desoxycorticosterone acetate are its low cost its high constant potency and its stimulation of sodium chloride retention Disadvantages of the drug lie in the danger of overdosage which may produce hypertension edema or cardiac failure This synthetic hormone does not affect the pigmentation present in Addison s disease neither does it influence the carbohydrate metabolism

Manifestly no set rule of treatment of fixed dosage schedule can be given The changes in the course of therapy must be mediated through the individual s response Adequate treatment will result in

and prostration result There is good evidence to the effect that the bends is due chiefly to the interruption of blood supply in bone as a result of nitrogen emboli and aseptic necrosis of the bone

The second most common symptom is vertigo known to the workers as the staggers The symptoms resemble those of Ménière s syndrome Vertigo may be so severe as to be accompanied by staggering nausea or nystagmus and tinnitus A worker seen in this condition resembles a man under the influence of an excess of alcohol he may be thought to be an alcoholic and treated as such unless his identification is seen Vertigo and its accompaniments are thought to be caused by the evolution of nitrogen bubbles in the labyrinth cochlea and semicircular canals

Many patients develop neurologic manifestations of a serious nature The nervous disorder produced may simulate almost any other disease or injury of the spinal cord There may be collapse and complete unconsciousness or simply numbness and tingling of the extremities Paralysis of the bladder and bowels is common in spinal cord cases Permanent weakness of the lower limbs may result Hemiplegia monoplegia strabismus nystagmus diplopia paresis and sensory disturbances occur

Dyspnea or the chokes is characteristic of another group of patients The condition is due to the accumulation of gas in the large veins the right side of the heart and the pulmonary vessels and may occur several hours after relatively normal decompression The chokes may begin as a sensation of mild substernal distress Gradually dyspnea results and the skin becomes cyanotic or ashen and clammy Paroxysmal attacks of coughing occur and ultimately loss of consciousness ensues The terminal picture is that of circulatory collapse

There may be cutaneous manifestations known as the itch Erythema mottling and pruritus are seen Pruritus is intense Cutaneous signs are usually early manifestations of compressed air sickness and signify possible ensuing symptoms of great severity

Prognosis The mortality of caisson disease has dropped to a low figure because of the efficiency of the recompression treatment In cases of sudden collapse and unconsciousness the prognosis is graver than in those presenting only pain in the extremities Where paralysis is present cure is difficult and advice as to the outcome should be guarded Manifestly the prognosis is considerably better

case alcoholism and fatigue predispose an individual to caisson disease

An associated pathological condition in compressed air sickness is so called ear block and its variant sinus block Acute upper respiratory infections are troublesome in compressed air labor because such infection frequently involves the eustachian tubes and ostia of the sinuses On entering the compressed air chamber the ear drum is stretched with resultant pain known as ear block due to the failure of the eustachian tubes to open and equalize the pressure on either side of the tympanic membrane If the pressure is great enough the result may be rupture of the tympanum and infection of the middle ear Similarly infection of the mucous membrane of the ostia of the sinuses may cause edema and the formation of a valve like action which allows air to enter the sinus but not to escape Air becomes trapped in the sinus under pressure causing sinus block

Pathology As the result of sudden decompression the dissolved gas is released as bubbles in the blood the various tissue fluids and in the fat depots and minute emboli are formed particularly in the brain the spinal cord the bone marrow and the bones Numerous small infarcts are produced and in the lumbar and thoracic cords areas of necrosis and softening with degeneration and destruction of the fibers are seen Fatal cases have been separated into a rapidly fatal and a delayed fatal group In the former death has been thought to be caused by nitrogen emboli in the vital centers of the brain in the coronary vessels and in the pulmonary arteries In the group of delayed deaths fatalities are supposedly caused by secondary complications following neurologic manifestations of the disease

Signs and Symptoms Three chief phenomena result from rapid decompression These are pain paralysis and asphyxia The onset is relatively rapid and the symptoms in 60 per cent of cases appear within the first hour after release from the abnormally high pressure in 30 per cent of cases in the second hour and in 5 per cent within three hours or more The most common manifestation of compressed air illness is pain which varies in intensity according to the site of the bubble formation and the amount of gas released It is usually a dull throbbing type of pain shifting in character is frequently felt in the joints but may be felt in the muscles and bones Abdominal pain may occur and may be of such severity that collapse

gases hasten the elimination of dissolved nitrogen from the blood Strychnine epinephrine and caffeine are valuable in cases of circulatory collapse For respiratory failure artificial methods should be used Physical therapy and nursing care should be used as indicated Hot packs may be applied to the affected parts

ACUTE ALTITUDE SICKNESS

Acute altitude sickness is the result of a decrease in the partial pressure of oxygen in the inspired air at high altitude and is characterized by acute anoxia with its corresponding symptom complex

Etiology In rapid ascent from normal atmospheric pressure to the rarified atmosphere at high altitude increasingly lower partial pressure of oxygen is encountered For example at 18 000 feet barometric pressure is reduced by one half that of sea level and the partial pressure of oxygen is correspondingly reduced by one half Consequently the hemoglobin of the blood is only 70 per cent saturated in comparison with the normal of 97 per cent The result is anoxia

Signs and Symptoms The signs and symptoms of anoxia are typical and vary with the degree thereof The first evidence is an increase in the respiratory and pulse rates with the occurrence of a mild headache Subsequently there is mild euphoria succeeded by retardation of mental and physical processes reduction of acuity of the special senses pronounced fatigue occasionally personality changes and ultimately loss of consciousness

Prognosis The condition is usually a temporary one although after effects may remain such as headache nausea vomiting and lethargy Complete recovery from any single exposure usually takes place in 24 to 48 hours After repeated exposures to high altitude a chronic fatigue like state often takes place remediable only by prolonged rest

TREATMENT

The actual treatment of individuals exposed to altitude sickness is a return to normal atmosphere A more logical approach to the anoxia of high altitude is prevention by methods currently in use i e the employment of oxygen through suitable masks or the pressurization of aircraft cabins Individuals with diseases rendering them susceptible to oxygen depletion should be advised to avoid high

if immediate steps are taken to effect recompression upon the development of symptoms

TREATMENT

1 **Prophylaxis** There is no immunity to caisson disease The most important step in prevention is the physical examination with special emphasis on the lungs, circulatory system and cardiac reserve Age, weight and habits should not be overlooked A man who shows symptoms of the disease after one or two trial tests should be rejected from this type of work though repeated mild attacks of pain and itching should be no cause for rejection

The ultimate prevention of the disease depends on the proper elimination of nitrogen from the tissues during decompression Nitrogen must be eliminated through the lungs by the circulation The value of exercise during the decompression stage to stimulate circulation should be stressed The necessity of slow decompression should also be kept in mind The working time under pressure should always be held within safe limits with adequate rest periods between shifts The use of helium oxygen atmosphere in compression work has assisted in the reduction in occurrence and severity of the disease Helium being an inert gas as is nitrogen acts by virtue of its lower fat solubility coefficient and its more rapid rate of diffusion Another advantage of helium is the fact that it does not produce the narcosis typical of nitrogen under pressure The inhalation of oxygen and oxygen helium mixtures during the decompression period to hasten the release of nitrogen is likewise beneficial Sudden changes in temperature should be avoided

2 **Active Treatment** The essential treatment of a patient with active symptoms of caisson disease is return to the compressed air chamber and subsequent slow decompression Recompression should be started as soon as possible Symptoms which persist or are unrelieved may require a prolonged period of compression in some instances for 24 hours with slow decompression to effect suitable response It has been noted that if treatment is delayed a higher pressure is necessary for relief

Exercise of the affected limb during decompression aids materially in obtaining permanent relief Inhalation of pure oxygen and oxygen helium mixtures has given encouraging results as these

CHAPTER X

The Nervous System

VERTIGO

Vertigo or dizziness as it is so often called by the laity is merely a symptom denoting a variety of terms including such sensations as light headedness to true dizziness or vertigo

Etiology and Pathology One of the best classifications of the causes of vertigo is that given by Simonton stating that vertigo may occur in the course of cardiac renal or vascular diseases in pernicious anemia and severe secondary anemia as a result of anemia or hyperemia of the labyrinth More severe degrees are seen among patients suffering from leukemia or purpura whenever hemorrhage into the labyrinth occurs Toxic vertigo is caused by tobacco alcohol drugs (principally quinine and the salicylates) constipation acute infectious diseases and focal infections Nitrogen embolism such as seen in divers or caisson workers and more recently among pilots of fast climbing fighter airplanes is a cause of vertigo Vertigo may also be produced by allergic hypersensitiveness Ocular vertigo results from a sudden paralysis of the ocular muscles Expanding lesions of the cerebellum or cerebellopontine angle such as tumors cysts or abscesses or vascular anomalies pressing on the acoustic nerves induce a constant type of vertigo Disseminated sclerosis with involvement of the cerebellum or vestibular centers may cause vertigo Trauma such as blows on the ear produces rupture of the tympanic membrane or hemorrhage into the middle ear Basal skull fractures involving the labyrinth are causes of vertigo Concussions produce the condition by injury to the vestibular nuclei Acute closure of the eustachian tube or a sudden closure of the external auditory canal may cause auditory vertigo Infections of the labyrinth invariably produce vertigo this type is usually very severe and continues during the acute stage and gradually diminishes as the acute inflammation subsides

Ménière s disease is characterized by recurring attacks of vertigo associated with tinnitus and deafness of the perceptive type Nausea

altitude flights without continuous oxygen inhalation Such instances are coronary heart disease pulmonary fibrosis emphysema therapeutic pneumothorax and the like

Other problems met with in high altitude aviation are those of decompression sickness cold expansion of gases and acceleration Decompression sickness occurs in a manner identical with that of caisson disease and is due to production of nitrogen bubbles upon rapid reduction of atmospheric pressure The condition is commonly referred to as aeroembolism and may be manifested by the bends chokes cutaneous disturbances such as parasthesia and rashes circulatory reactions and neurologic symptoms

Expansion of gases is met with chiefly in aerootitis media in which difference in pressure occurs between the external air and air in the middle ear due to lack of patency of the eustachian tube The condition is identical with that of ear block or sinus block of caisson disease

The problem of cold in aviation differs very little from that in other circumstances other than in the matter of degree and the increased need for efficiency At a cockpit temperature of 0° F there is a 30 per cent loss of efficiency due to frosted goggles cold hands and feet or perhaps even frostbite and clumsiness from heavy clothing and this percentage increases as the temperature decreases The problem is now largely eliminated through the use of enclosed heated cockpits heated cabins and electrically heated flying suits

Acceleration defined in physics as the rate of change of velocity has posed a constantly mounting problem in aviation medicine particularly with the advent of jet and rocket propelled aircraft The effect of acceleration is most commonly seen in the so called black out which occurs typically in sharp turns at high speeds The mechanism is due to the action of centrifugal force on the blood stream There is alteration in rate and direction of flow of blood in arteries veins and capillaries and acute anoxia takes place Extensive study is being carried on to determine the tolerance of the human body to these unusual conditions with an eye to their elimination or prevention

variable since the individual patient s response varies in almost each instance

TREATMENT

The treatment must always be directed toward the removal of the pathological cause

1 The transient vertigo as that caused by car sickness and toxic vertigo are quite readily relieved with the removal of the offending agent plus dehydration by means of saline cathartics as magnesium sulfate 16 Gm (4 drams) daily for three days restriction of fluid and induced sweating In addition a spinal puncture and the intravenous injection of 50 cc of 5 per cent glucose solution may bring about a cure

2 Vertigo due to intracranial lesions is of course treated directly by way of surgery

3 Vertigo caused by nitrogen embolism is treated by gradual decompression in the chamber or it may be prevented by individual s inhalation of pure oxygen prior to the sudden lowering of the air pressure

4 Ocular vertigo such as occurs following a sudden paralysis of one of the extraocular muscles can be immediately corrected by closing or covering one eye

5 In general the treatment of vertigo subsequent to trauma is purely symptomatic

6 The treatment of infectious labyrinthitis should be conserva tive during the acute stage and should extension of the infection beyond the labyrinth occur an operation on the labyrinth should be done When the disease has reached the quiescent stage a labyrinthec tomy offers the surest protection against recurrence and extension of the inflammation should the infection be a purulent one

7 Meniere s disease may be treated as follows

a The Furstenberg regimen which includes the elimination of extra salt in the diet plus the substitution of ammonium chloride 3 Gm (45 grains) in capsules with each meal three days on and two days off to maintain the chloride level of the body

b Nicotinic acid 50 mg ($\frac{5}{6}$ grain) three times a day thiamine chloride 10 mg ($\frac{1}{6}$ grain) three times a day which acts as a vasodilator

c Histamine diphosphate in a dose of 2 75 mg in 250 cc. of normal saline solution given intravenously at the rate of 40 to 60 drops per minute for 10 days Occasionally the patient will note a slight sensa

vomiting and spontaneous nystagmus usually accompany the attacks *Only rarely does the patient lose consciousness although he may* collapse Hypersensitive carotid sinus may frequently arise through vertigo which actually is more of a syncope than a true vertigo In this instance stimulation of the sensitive carotid sinus causes a stimulation of the vagus which in turn slows the heart thereby producing cerebral edema

Hallpike and Cairns have pointed out that the pathologic findings in aural vertigo show gross dilatation of the endolymph system of the internal ear Dandy on the other hand feels that the condition is due to pressure by an abnormal vessel upon the eighth nerve The pathologic conditions associated with vertigo without auditory symptoms *or central neurologic signs are not known although when of peripheral* origin it has been explained on the basis of labyrinthitis of various types

Signs and Symptoms Vertigo may vary as to its intensity It may be nothing more than a transitory feeling that objects are rotating in space or it may be a sensation of violent rotation to such a degree that the patient may be thrown to the ground because of his inability to orientate himself with his immediate environment Vertigo of any intensity at all may cause staggering when the individual attempts to walk or if operating a vehicle there may be difficulty in keeping it in its proper line Nausea and vomiting may occur in true vertigo depending upon the severity of the disorder Vasomotor symptoms such as pallor and cold sweat may accompany vertigo

Diagnosis Diagnosis of aural vertigo is not difficult if a careful *history is derived and if cerebellopontine angle lesions are ruled out*

Prognosis Prognosis depends on the underlying cause Vertigo resulting from sea or car sickness disappears with the elimination of the cause—that is the uneven motion Toxic vertigo may be alleviated by the removal of the offending agent The vertigo due to labyrinthitis when serous or purulent is always accompanied by a grave prognosis due to the pathway which is present for the extension of the infection directly to the meninges of the brain In intracranial lesions such as cerebral tumors or tumors of the cerebellopontine angle one usually sees a disappearance of the vertigo following removal of the tumor The prognosis in Ménière's disease is

3 Constitutional intoxications or metabolic conditions as diabetes uremia eclampsia and hypoglycemia responsible for about three per cent
4 Epilepsy 2 5 per cent.
5 Toxic conditions as pneumonia and septicemia of various kinds causing 1 5 per cent
6 Cardiac decompensation Stokes Adams syndrome coronary thrombosis, and the like causing 1.5 per cent
7 Miscellaneous causes which include such conditions as cholemia ruptured ectopic pregnancy miliary tuberculosis hysteria and massive hemorrhages, accounting for four per cent of the causes of coma

The relative frequency of coma due to each of these varies with one s type of practice Internists see many cases of coma due to acidosis diabetic coma or hypoglycemia Industrial surgeons may see skull injuries while a neurologist may see more comas due to epilepsy cerebral vascular accidents or brain tumors There are many causes of coma and they are so varied that all cannot be mentioned It is not important to carry all of the possibilities in mind but one must have the basic causes classified Age is always of first consideration In a patient under 40 diseases like epilepsy and infection are common in older individuals metabolic disorders cardiovascular disease and tumors of the brain occur more frequently Aside from hemorrhage few things frighten the public as much as coma If a patient is in coma the first step is to determine the cause of the trouble History is essential It may be obtained from anyone who has been with the patient or occasionally from the patient himself if he can be aroused or possibly if he has a lucid period Trauma either immediate or remote must be considered in every case A patient may suffer injury to the head and not lapse into coma until weeks later when a subdural hematoma develops In a patient who has been well and is suddenly taken with fever chills and rapid pulse infection with some bacterial agent must be kept in mind Poliomyelitis meningitis or any inflammatory lesion of the brain or its appendages must be considered

Signs and Symptoms In discussing coma each of the main groups will be analyzed separately and the outstanding findings on physical examination and clinical course given

1 *Acute Alcoholic Intoxication* This type of coma is very common The patient is sound asleep but is seldom so comatose that he cannot be aroused sufficiently to answer questions unless

tion of heat in the face headache and rapid increase in pulse rate but this can be controlled and recurrence avoided by reducing the rate of flow Treatment is continued from three to six days Following the injections subcutaneous administration of histamine 0 275 mg (1/240 grain) one to four times weekly is recommended for an indefinite period to maintain beneficial results If evidences of histamine reaction occur following administration of a maintenance dose the dosage is reduced 50 per cent later an attempt is made to increase the dosage Histamine therapy has improved hearing and relieved vertigo and tinnitus in many cases of Ménière s

d Pyridoxine 100 mg a day in divided doses either orally or intravenously has been used by some authors

e Division of the auditory nerve if medical treatment fails

8 Should the carotid sinus be the cause of vertigo and simple measures as the elimination of high stiff collars and sudden twisting or stretching of the neck are not effective it may be necessary to do a denervation of the hypersensitive carotid sinus to obtain relief

COMA

Coma presents one of the most interesting and dramatic episodes in medicine It may be defined as a loss of consciousness from which the patient cannot be aroused by the application of the most powerful external stimuli The commonest etiological factors to be considered in the differential diagnosis of coma may be grouped in simple classifications as included in the following table Cases of diabetic coma insulin reaction poisoning and others require *immediate* treatment

Etiology The causes of coma in patients entering a hospital in order of frequency are

1 Poisonings
   - *a* Alcoholic which is responsible for 59 per cent of cases in large urban hospitals
   - *b* Barbital poisoning cocaine opium carbon monoxide bromides lysol causing three per cent
2 Cerebral lesions
   - *a* Trauma *which causes approximately 13 per cent*
   - *b* Cerebral vascular lesions as hemorrhage thrombosis and embolism causing about ten per cent
   - *c* Tumors central nervous system syphilis and inflammations of the brain and encephalitis causing approximately 2 5 per cent

great care in the presence of choked disks Sudden death due to jamming down of the medulla oblongata into the foramen magnum may follow puncture in such cases

3 *Intoxications or Metabolic Conditions* The diagnosis is based on a history of diabetes nephritis pregnancy or use of insulin The diabetic patient who is in acidosis either knows he has diabetes or gives a suggestive history of diabetes such as polydipsia polyuria polyphagia loss of weight or a history of frequent infections which resist ordinary treatment Such information may be obtained from the family or occasionally from the patient himself

This condition is unlike insulin reaction Usually a slow pulse soft eyeballs Kussmaul air hunger clammy skin and the odor of acetone on the breath are evident However it must be remembered that the odor of acetone on the breath or the presence of it in the urine may mean dehydration and not necessarily diabetic coma The urine may show glycosuria acetone and acetoacetic acid Typical hypoglycemia may be revealed by determination of the blood sugar at times the eyegrounds show diabetic retinitis The absence of glycosuria does not necessarily indicate the absence of diabetes because a recent injection of insulin may have controlled the excretion of sugar even though a severe acidosis is present In insulin shock the patient is irritable sweaty and the skin is warm The pulse is rapid and nervousness hypotension and tremor predominate The pupils are dilated In the laboratory tests the urine shows no sugar although it may be found if the urine has been retained in the bladder for several hours The blood pressure may be elevated

Uremic coma is the result of renal insufficiency Renal failure may be due to nephritis pyelonephritis renal tuberculosis or any condition which interferes with the proper secretion of urine It is customary to classify uremic coma into the (1) genuine and (2) convulsive types Although both kinds may occur together in the same patient the causes of these episodes are different Genuine uremia is the result of renal failure and the accumulation of toxic products in the blood and tissue Convulsive uremia on the other hand is not dependent on renal failure at all but on hypertension and increased intracranial pressure

4 *Epilepsy* This individual may be one who has been known to have had attacks in the past The history from relatives is very

the alcoholism is complicated by another disorder In the typical case the patient has a flushed face a florid appearance an alcoholic odor to his breath the pupils are dilated and the conjunctivae are injected If alcoholism is chronic the typical red nose is prominent. The most commonly associated complications are skull fracture or poisoning by the various impurities as lead or methyl alcohol which may have been present in the alcohol consumed

2 *Cerebral Lesions* The commonest cause is trauma and the most important factor in the diagnosis is the history of direct injury to the head Symptoms referable to cerebral concussion compression irritation or paralysis are often the main factors laboratory findings as x ray or spinal fluid will aid in making a positive diagnosis However it must be remembered that any individual with a head injury may have a skull fracture with or without symptoms Therefore it is difficult to determine in trauma whether or not a skull fracture is present Any patient with an acute head injury must be considered a potential skull fracture case until it is proved otherwise As stated above the symptoms may be latent for several weeks until pressure due to a subdural hemorrhage occurs

The patients with cerebral vascular lesions are of various types The young individual one under the age of 40 may present himself in coma he probably has an embolus caused by a fibrillating heart or a rupture of congenital or mycotic aneurysm of the cerebral artery The individual between 40 and 60 years of age with high blood pressure and arteriosclerosis may present himself with a thrombosis or a hemorrhage The symptoms are characteristic though they may resemble each other There may be no history of trauma There is usually a flaccid paralysis a Babinski sign may be present and as the patient breathes the paretic cheek blows out and drops lower than the normal one There is a deviation of the eyes and the superficial reflexes are lost on the side of the lesion Finally the spinal fluid may or may not show the presence of blood

Brain tumors and central nervous system syphilis are recognized with increased frequency In brain tumors the onset is usually gradual with a history of headaches failing vision dizziness and vomiting and finally the patient passes into coma he may have choked disks and other localized signs Increased intracranial pressure may call for spinal puncture although this must be done with

of infection is present, one must take a blood culture and when central nervous system syphilis is suspected a blood Wassermann and spinal fluid serology should be done The nonprotein nitrogen and carbon dioxide combining power of the blood should be determined Lumbar puncture must be routine in all injuries (except during shock) cerebral vascular accidents convulsions in the presence of signs of increased intracranial pressure or meningeal irritation and in all cases where the diagnosis is obscure The initial pressure the color of the fluid red and white blood cell count spinal fluid protein and serology are considered Enough fluid should be saved for smear culture and pellicle formation Finally one must be reminded again that if the above tests fail the clinical course frequently discloses what the tests do not reveal

TREATMENT

1 *Central nervous system lesions*

a Extracranial lesions

(1) When a diagnosis of head injury is made and the extent of the lesion determined there are several don ts to be observed

(*a*) Do not move the patient for x rays If it is essential to determine the extent of various compound fractures portable x ray apparatus should be used

(*b*) Do not operate in shock unless the shock is due to a bleeding meningeal artery or unless the bleeding must be controlled to stop shock.

(*c*) Do not dehydrate in shock It is permissible to treat shock with intravenous injections of isotonic solutions of glucose or saline Hypertonic solutions should not be given in the presence of dural or extradural hemorrhage

(*d*) Morphine should not be given as a routine measure because of the masking of symptoms and signs which may occur and also because of the respiratory depression

(2) The following treatment is indicated

(*a*) The patient should be put into a shock bed

(*b*) External heat is applied

(*c*) The room should be kept dark and quiet and visitors restricted.

(*d*) All bleeding vessels should be sutured or bleeding controlled by applying pressure dressings

(*e*) All fractures should be immobilized by the use of sandbags or temporary splints In the presence of depressed and compound fractures surgical intervention is necessary

important it will be that of a typical grand mal attack preceded by an aura after which the patient cries out falls and has tonic and clonic convulsions together with involuntary passage of urine and feces and then goes into a comatose state One may find evidence of injury to the tongue or buccal mucous membrane It must be remembered that these individuals may suffer severe head injuries when they fall

5 *Toxic Conditions* The most important point in establishing this as a cause of coma is the history of infection the presence of high fever and leukocytosis and the history of chills

6 *Cardiac Decompensation* Here again the patient s past history and the physical examination will determine the diagnosis

7 *Miscellaneous* This group has to be considered only after all of the above have been ruled out

Diagnosis Diagnosis must be made carefully and accurately Physical examination frequently establishes the diagnosis If one uses his five senses an obscure diagnosis may often become very obvious An odor of alcohol acetone gas or a uriniferous odor may be suggestive Injury to the skull bleeding mouth or a laceration of the tongue may indicate the etiology Other valuable aids may be found on examination as needle marks seen in a narcotic addict the presence of a diabetic regulation card morphine tablets lumps of sugar or syringes The presence of a dilated pupil on one side or the other high blood pressure or neck rigidity may also give one an important clue as to diagnosis

Fundoscopic examination may reveal the presence of intracranial tumors albuminuric or diabetic retinitis which may prove the presence or absence of any of these conditions One must also look for rigidity of the neck fractures muscle and vasomotor tone in the extremities and enlarged glands Finally the examination of the heart and lungs and the evaluation of the temperature pulse respiration and blood pressure must be considered If the above fail the subsequent clinical course frequently reveals what has been obscure in the initial examination

The next procedures are the laboratory examinations which should start with urinalysis and blood counts followed by gastric lavage in all cases of suspected poisoning and severe alcoholism All the contents must be saved for chemical examination If evidence

(f) Rapid irregular and stertorous respiration usually accompanies serious injuries

(g) Lucid interval may mean subdural or extradural hemorrhage or cerebral edema Convulsions and localizing symptoms may occur from cerebral edema and disappear with a few hours if they are due to edema alone

(h) The question of spinal taps has long been a disputed point They should not be done in subdural or extradural hemorrhage intracranial hemorrhage or severe shock Diagnostic taps may be done to determine pressure and the presence of blood However only 1 or 2 cc of fluid should be removed. If spinal taps are done for treatment sufficient fluid should be removed to reduce the spinal fluid pressure to one half of the original pressure

(4) Prognosis Patients with severe injuries should be hospitalized for from two to six weeks depending upon the symptoms The length of bed rest can be determined by the patient s condition The patient is allowed up after he has been symptom free for a few days If headaches and dizziness develop after the patient is up and about he should be put back to bed for a few more days of rest

b Intracranial Trauma A patient who develops a stroke must always be treated quickly and with precision This emergency may arise at any time any place and under almost any circumstances The patient who has a hemorrhage of the brain is most likely to give the true picture of an apoplectic stroke This disorder usually occurs in a middle aged individual who has had high blood pressure The onset of hemorrhage is abrupt and is precipitated usually by exercise or straining particularly by forced expiration with a closed glottis which increases the pressure in the vascular system of the brain Occasionally however a cerebral hemorrhage occurs while the patient is at rest

The emergency treatment of a patient with a stroke is simple but very important At first too energetic treatment may increase the hemorrhage aggravate the symptoms and cause death

If heart failure is present digitalis should be given intramuscularly or intravenously Thromboplastin 20 cc. or 2 cc. of the patient s blood may be given intramuscularly Later drugs as theobromine 0 33 Gm (5 grains) three times a day or potassium iodide 0 6 cc (10 minims) five times a day may be given

c Cerebral diseases The treatment of brain tumors of course is surgical Central nervous system syphilis may be treated by fever therapy malaria treatment or tryparsamide When a diagnosis of meningitis is made the patient should be treated with the available specific sera and with the sulfonamides (see page 393) In the treatment of epidemic encephalitis the patient must be kept in bed and restraints applied if necessary Symptomatic treatment is used as symptoms arise Opiates should be administered with great caution The treatment of most

(f) All wounds should be débrided and sutured as soon as the patient is out of shock

(g) Extradural and subdural hemorrhage do not require immediate surgery *Surgery may be done when the patient s condition warrants the procedure* It should be delayed as long as it is deemed necessary and depends upon the findings as they arise

(h) Certain drugs may be used as atropine sulfate 0 45 or 0 65 mg (1/1 0 or 1/100 grain) strychnine sulfate 1 or 2 mg (1/60 or 1/30 grain) pituitrin (surgical) ½ to 1 cc intramuscularly cortin 10 cc intravenously or intramuscularly repeated at frequent intervals depending upon the degree of shock.

(i) Hypertonic solutions which are most commonly used are 50 per cent sucrose 100 to 200 cc. intravenously or 50 per cent glucose 50 to 100 cc intravenously Sucrose may be repeated in 12 to 24 hours but it should never be used in the presence of kidney damage Glucose may be repeated in 6 to 12 hours Fluids as normal saline or five per cent glucose 500 to 1000 cc should be given intravenously if the patient has lost considerable blood In some cases transfusion may be indicated

(j) For sedation the best drugs are chloral hydrate 2 Gm (30 grains) sodium phenobarbital 0 1 Gm (1½ grains) or sodium amytal 0 2 Gm (3 grains) Magnesium sulfate 30 Gm *(1 oz) by mouth or 60 Gm (2 oz) rectally* as a retention enema may be helpful

(3) Following these procedures the patient must be observed very closely for edema or hemorrhage

(a) Special attention should be paid to the state of consciousness restlessness the occurrence of convulsions and the patient s use of his arms and legs

(b) Careful neurological examination should be repeated frequently to note any changes It must be remembered however that many abnormal findings may be temporary after convulsions and they do not necessarily mean that the patient *is showing any progression of hemorrhage*

(c) Blood pressure readings should be taken every one or two hours A drop in diastolic pressure below 60 mm of mercury means shock Systolic pressure above normal may be a sign of edema of the brain or increased intracranial pressure

(d) The pulse must be watched carefully Slowing of the pulse to 60 beats or less a minute may mean cerebral edema A very rapid or irregular pulse is a bad prognostic sign in that it shows that the patient has difficulty compensating for his injury

(e) The temperature is subnormal in shock and later in severe injuries begins to rise this is a bad prognostic sign especially if it reaches 40 5 to 42 2 C (105 to 108 F) within a few hours after injury

(12) If acidosis is extreme as evidenced by a low carbon dioxide combining power the use of 500 cc 6/M sodium lactate solution intravenously will counteract this
(13) As a last resort, surgical decapsulation of the kidney in extreme coma and anuria is indicated
(14) The method of delivery of the fetus is left to the judgment of the obstetrician Some authorities favor conservative treatment allowing the patient to continue to term while others favor the emptying of the uterine contents as soon as possible without violence through version forceps or cesarean section

3 *Epilepsy* Epilepsy may be treated in an institution or in the home The patient s general habits and occupation need supervision The drugs for chronic use are bromides phenobarbital and dilantin sodium The dosage must be decided for each individual case but it should be remembered that when bromides are used sodium chlorides should be administered because bromides and iodides hasten the elimination of chlorides from the body The patients taking the barbiturates or dilantin are usually more alert than those on the bromides

4 *Toxic conditions* The treatment of these causes of coma is directly dependent upon the treatment of the original conditions

5 *Miscellaneous causes* Probably the commonest of these are heat exhaustion and sunstroke Heat exhaustion presents symptoms similar to shock while patients with sunstroke have a high fever a rapid full pulse and high blood pressure They become restless and excited and later develop delirium The treatment of these conditions is discussed on page 216

CEREBRAL HEMORRHAGE EMBOLISM AND THROMBOSIS

Cerebral hemorrhage thrombosis and embolism are vascular accidents involving the arteries of the brain and are generally grouped together under the term apoplexy The differentiation between these kinds of apoplexy is of little importance as far as the treatment of the patient is concerned Thrombotic lesions are commonest of all cerebral accidents due to hemorrhage come next Patients with cerebral hemorrhage are more apt to die in the acute attack while those with thrombosis survive the acute phase though they sustain considerable disability as partial hemiplegia When a cerebral accident is caused by syphilitic arteritis the patient is usually young and the condition is amenable to proper treatment Thrombosis may involve almost any of the main cerebral vessels either those comprising the circle of Willis and its branches or the anterior middle and posterior cerebral cortical arteries Hemor

value seems to be repeated lumbar punctures to relieve the stupor headache and cranial nerve palsies The sequelae of the disease as tremor and the parkinsonian syndrome should be treated with stramonium compounds The treatment of patients with hysterical attacks is purely psychiatric

- *Intoxications of metabolic origin*

a Diabetic coma and insulin shock (see Chapter VIII)

b Uremia (see Chapter XII)

c Eclampsia The treatment of this condition is of course the prevention of the disorder by prenatal care and observation However if the clinician is called to see a patient in the last trimester of pregnancy with sharp epigastric pain disturbed vision or severe headaches followed later by twitchings convulsions dyspnea edema high blood pressure or albuminuria then the treatment must be energetic

(1) The patient is put to bed at absolute rest in a warm dark room

(2) Sodium luminal 0 13 or 0 2 Gm (2 or 3 grains) or morphine sulfate 0 016 to 0 032 Gm (1/4 to 1/ grain) hypodermically is given immediately The administration of the drugs should be repeated in two hours if necessary to control the convulsions

(3) The patient must be protected against injury and all mucus must be removed from the mouth

(4) Control of the convulsions may also be secured by the intravenous administration of 20 cc of ten per cent solution of magnesium sulfate Four doses are usually enough and up to 8 Gm (120 grains) as a total dose is sufficient Magnesium sulfate as an eight per cent solution may also be given intramuscularly up to a total of 2 Gm. (30 grains) per kilogram of body weight or as a slow drop by drop enema 20 Gm (300 grains) in 1/2 to 1 liter of water

(5) Phenobarbital hypertonic solutions as 50 per cent glucose or sucrose may be given intravenously for control of convulsions

(6) To maintain fluid balance and keep the blood pressure down constant and copious withdrawals from the bowel and bladder are indicated as well as venesection and bandaging of the extremities

(7) All foods and fluids by mouth are withheld for 24 hours

(8) Oxygen inhalations are given after each convulsion until the breathing is normal and the cyanosis disappears

(9) The circulation should be stimulated by the use of metrazol 0 2 Gm (3 grains) hypodermically

(10) The patient should be given a daily purge with magnesium sulfate 15 to 30 cc (1/ to 1 oz) by mouth

(11) Diuresis should be established Hypertonic glucose 300 cc. of 25 per cent solution should be administered intravenously every four or five hours during the attack Mercurial diuretics as salyrgan 1 cc by vein are used

releasing of a small thrombotic mass from the left auricle during auricular fibrillation and heart failure

According to Turnbill the first change in the arteries is hyper trophy of the media which has undergone degeneration and atheroma of the intima occurs as a result of high blood pressure and degenera tion

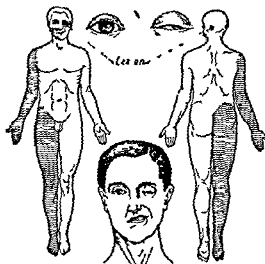


Fig 2—1 Paralysis of the extremities on the side opposite the brain lesion 2 Oculomotor paralysis on the same side as the lesion (a) Ptosis (b) Outward deviation of the eye owing to persistence of function of the fourth and sixth cranial nerves.

Signs and Symptoms The onset is usually abrupt *during strenu ous exercise* while at rest or sometimes while performing an ordi nary duty Occasionally there may be premonitory symptoms of headache numbness or tingling in the limbs and choreiform move ments in the muscles of the opposite side of the body Sometimes vascular disturbances are described by the patient after recovery Transient aphasia or monoplegia may occur occasionally When the onset is sudden consciousness is lost and complete relaxation of the extremities occurs Subsequently whether the onset is sudden or gradual the face usually becomes cyanotic or ashen-gray the pupils vary in size commonly being dilated and frequently unequal and unresponsive to light *When the lesion is in the pons or in the ventricles* the nucleus of the third nerve is irritated and constric

rhage occurs in the lenticulostriate of the middle cerebral so frequently that this vessel has been called the artery of cerebral hemorrhage

Etiology and Pathology Apoplexy due to cerebral hemorrhage is practically always caused by hypertension It usually occurs in people past 45 years of age when arterial degeneration accompanies hypertension

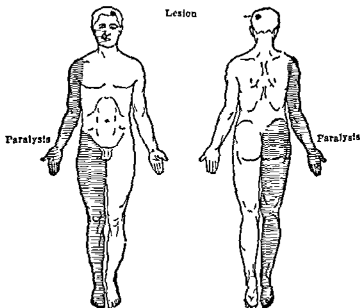


Fig 1—Hemiplegia of cerebral origin Paralysis of the lower branch of the facial and of the extremities on the side opposite the lesion

tension The hemorrhage of a mycotic aneurysm may occur at any age and simulate closely apoplexy of hypertension Mycotic aneurysms have a predilection for the circle of Willis at the junction with the anterior cerebral Apoplectic strokes due to hemorrhage are more apt to occur in individuals who indulge in alcoholic excesses and in those who overeat or participate in excessive muscular exercise

Apoplexy caused by cerebral thrombosis nearly always develops in older persons who have generalized hardening of the arteries In these cases the onset is less abrupt and several days may pass before the full effects of the thrombotic occlusion are witnessed The apoplectic stroke of cerebral embolism may occur at any age and is caused by such diseases as vegetative endocarditis, abscess of the lung bronchiectatic cavitation or probably commonest of all the

part of the pons The facial paralysis results in difficulty or inability *to elevate the eyebrow close the eye or move the corner of the* mouth When the hypoglossal nerve is involved the extension of the tongue will show deviation toward the paralyzed side In addition various degrees of aphasia and aphonia may occur due either to involvement of these areas within the brain itself or the muscles controlling these functions In most instances a permanent paralysis results and certain groups of muscles are more likely to be affected permanently than others In the leg the flexors and the dorsal flexors of the foot are most frequently involved whereas the extensors of the leg and plantar flexors of the foot usually recover In the arm the muscles which oppose the thumb are usually affected as well as those which rotate the arm outward

Crossed hemiplegia occurs when the lesion is in the pons the crus or the medulla When the lesion is in the crus the condition produced is known as the syndrome of Weber and is characterized by paralysis of the arm face and leg of the opposite side and the third nerve on the same side In addition frequently there will be sensory changes When the lesion is in the pons or medulla the pyramidal tract will be involved and very likely one or more of the cerebral nerves Paralysis of the face on the same side and hemiplegia on the opposite side occurs when the lesion is in the lower part of the pons The external rectus muscle is usually also involved due to paralysis of the sixth nerve When the fifth nerve is involved there is loss of sensation on the same side as the lesion and loss of motor activity on the opposite side of the body

The Reflexes When the patient is in coma the knee jerks and abdominal reflexes are frequently absent on both sides and there is a positive Babinski On the hemiplegic side the lost reflexes may never return or they may come back very gradually

Diagnosis For practical purposes a general course may be outlined for all apoplectic strokes *In any and all cases there may be a* period of unconsciousness or partial lack of consciousness at the beginning which lasts for a few hours up to a few days Hemorrhage is more apt to produce an extensive period of coma which when seen is difficult to differentiate from other types of coma

Recently Gilbert and de Takats have differentiated apoplexy into cerebral hemorrhage thrombosis and embolism A diagnosis of

tion of the pupils occurs The respirations are stertorous slow and frequently Cheyne Stokes in type The pulse is slow and full The temperature may be subnormal or normal in basilar hemorrhage it may be elevated Incontinence of urine and feces usually occurs Physical examination will reveal that the affected side is flaccid that is when the limb is raised it will drop back on the bed as if dead Conjugate deviation of the eyes also develops in many cases

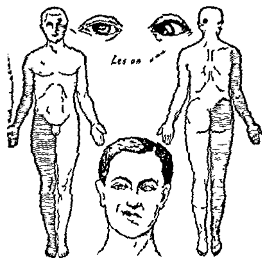


Fig 3—1 Paralysis of the extremities on the side opposite the brain lesion 2 Paralysis of the face on the same side as the lesion 3 Paralysis of the sixth cranial nerve on the side of the lesion causing convergent strabismus through deviation of the eye inward and downward.

When the onset is more gradual the patient may not lose consciousness but there will be a loss of power or complete paralysis of the affected extremities In some of these cases unconsciousness will occur later After the patient has recovered consciousness there may be hemiplegia either partial or complete This may persist for a variable period of time and completely clear up or never clear up at all depending on the location and extensiveness of the lesion

Hemiplegia After the patient regains consciousness a paralysis may be present The extent of this paralysis depends upon the degree of destruction that has occurred in the motor area in the pyramidal tract or in any part of its course Ordinarily the face is involved on the same side as the arm and leg unless the lesion is in the lower

elapsed for it requires this length of time to determine the degree of recovery that will take place Generally the recovery after the two month period is slight

TREATMENT

The emergency treatment of the patient with a stroke is simple but important Too energetic treatment may lead to more hemor rhage aggravate the symptoms and cause death The therapeutic measure called masterful inactivity is often the best method of treating the patient with a stroke The anxiety of the family to have something spectacular done often leads to overtreatment

1 The first step is to place the patient on a couch or mattress with his head elevated so foreign material will not be sucked into the trachea and lungs The breathing is usually better too if the patient is in a semireclining position It is important to keep the chin from falling onto the chest for this makes breathing difficult causes congestion in the veins of the neck increases the cerebro spinal pressure and promotes the active bleeding in the brain

2 Do not move the patient immediately after the stroke It takes half an hour to an hour for the initial shock to subside During this time small injections of caffeine sodium benzoate 0 13 to 0 26 Gm (2 to 4 grains) hypodermically may be given to keep up the circulation and prevent peripheral vascular collapse

3 When the time is appropriate move the patient to bed at home or preferably to a hospital At this stage the treatment may determine the outcome Icebags placed around the head appear to be effective in controlling the hemorrhage in the brain Be sure that the urinary bladder is not distended The bowels should be emptied freely because this serves to reduce the blood pressure An icebag applied to the heart slows circulation

4 If the blood pressure is very high the veins of the neck dis tended and the face florid and cyanotic 500 cc of blood may be withdrawn If these symptoms are not present venesection should not be done

5 There has been a tendency to give hypertonic glucose and sucrose solutions in the early stage of apoplexy but intravenous solutions should not be given during this period

6 When the patient becomes conscious a small dose of mor phine 0 01 Gm (1/6 grain) or pantopon 0 01 Gm (1/6 grain) hypo

cerebral embolism is made when the patient shows a sudden cerebrovascular insult has had previous embolic episodes involving the brain or other part of the body and has clear spinal fluid with no elevation of pressure The patient s age is also usually lower than those affected by thrombosis or hemorrhage Cerebral thrombosis is a condition diagnosed by eliminating embolism and hemorrhage from the cause of stroke and is characterized by cerebral softening absence of increased intracranial pressure clear spinal fluid and absence of papilledema and engorgement of retinal veins If the blood pressure is elevated this is part of the hypertensive encephalopathy On the other hand cerebral hemorrhage may be diagnosed when one finds a history of a sudden onset stiff neck high white blood cell count bloody spinal fluid under increased pressure and deepening coma

Prognosis The degree of paralysis depends on the severity of the lesion in the brain but the extent of the original paralysis is no measuring stick of the completeness of recovery which may take place Sometimes the patient with the most complete paralysis during the first few weeks eventually makes the best recovery while the one who suffers only mild paralysis may die A physician should not attempt to make an accurate prognosis until six to eight weeks have

TABLE I—DIAGNOSTIC TABLE

	Hemorrhage	*Embolism*	*Thrombosis*
Cause	High blood pressure	Valves	Arteriosclerosis or syphilis
Age	40 to 60	Young	Old—arteriosclerosis Young—syphilis
Onset	Sudden	Sudden	Slow
Paralysis	Hemiplegia	Hemiplegia and aphasia	Partial
Convulsions	Yes	Rare	Yes
Coma	Yes	No	No
Prognosis	Fair	Poor	Poor

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6 *When the patient* becomes *conscious a small dose of mor*phine 0 01 Gm (1/6 grain) or pantopon 0 01 Gm (1/6 grain) hypo

dermically will relax him and favor the clotting of blood in the brain

7 If the blood pressure continues to rise during the early hours of the stroke sodium nitrite 0 03 Gm (½ grain) may be given subcutaneously and repeatedly This reduces the blood pressure slows circulation and promotes clotting at the points of hemorrhage

8 When the patient has recovered from the first stage of the stroke he must be kept quiet Avoid trying to make him swallow until the process of deglutition is under control because coughing or choking may aggravate the condition in the brain or a particle of food may be sucked into the lung and cause pneumonia

9 Massage may be started about the tenth day followed by passive exercise with gradual encouragement to perform active exercise with the extremities Contractures are difficult to prevent but this may be accomplished in many cases by application of casts extension devices and other appliances as individually needed

10 By blocking the cervical sympathetic trunk with procaine on the side of the lesion some patients with apoplexy have regained consciousness and speech as well as having motor improvement and conversion of flaccid into spastic paralysis

CHAPTER XI

The Nervous System

(Continued)

HERPES ZOSTER

Herpes zoster more commonly known as shingles is an acute dermatological manifestation of a neuritic disease characterized by vesicular eruption distributed along the course of one or more peripheral sensory nerves

Etiology The cause of the disease is still unknown A filtrable virus has long been suspected as being the etiological agent However it differs definitely from the virus which produces herpes simplex Other predisposing factors are evident because of its common association and occurrence in patients who have been (1) overworked (2) affected by certain drugs or poisons especially the heavy metals (3) ill from a chronic disease as generalized arteriosclerosis diabetes central nervous system syphilis or (4) exposed to chickenpox

Pathology *The most salient changes are noted in the posterior* spinal ganglia or cranial nerve ganglia which reveals a lymphocytic infiltration perivascularly or hemorrhage and round cell infiltration At times the posterior gray columns reveal the same process which would explain the prominent nerve degeneration as is seen in very severe cases Histological study of the cutaneous lesion shows an inflammatory process at the onset interepithelial vesiculation and edema during the vesicular stage and fibrosis and pigmentation with an atrophic epithelial layer during the healing stage

Signs and Symptoms The onset is usually acute and is that of general malaise and occasionally gastrointestinal upset This is followed by a slight fever and the development of a neuralgic pain along the course of the affected nerve The degree of pain is variable and at this time the underlying skin is found to be hyperesthetic Shortly thereafter an erythematous eruption appears Within three to five days these lesions develop into papules vesicles and vesiculo-papules They appear in successive crops along the nerve distribution and usually involve one or two nerves They are most commonly uni

lateral but at times a *bilateral involvement is noted* The vesicles tend to become confluent and are grouped in small areas the usual case having 2 to 12 of these groups The vesicular lesions persist for a week or ten days when they finally dry up form crusts, and resolve *Atrophic scarring is the usual remnant after healing is complete* Sequelae may be (1) a persistent postherpetic pain (2) blindness secondary to fifth nerve involvement or (3) motor root involvement producing paralysis especially when cranial nerves five or seven are *affected*

Diagnosis Diagnosis depends upon the appearance of neuralgic pain followed by cutaneous vesicular eruption with the characteristic unilateral nerve distribution

Prognosis Prognosis is good One attack usually results in an immunity, although cases of repeated attacks have been observed especially in patients with chronic debilitation

TREATMENT

Treatment for the most part is symptomatic but certain measures have been instituted in an attempt to treat the patient generally Various combinations of the following may be tried

1 *Push fluids orally Administer a high caloric high* vitamin diet

2 Proper elimination through the use of cathartics

3 An intragluteal injection of 10 cc of patient s *own blood may* be *given daily or 20 cc may be given every* other day *in the acute stage* This treatment is less useful after the acute stage has passed

4 Surgical pituitrin 1 cc intramuscularly daily for four days for pain or the administration of iodide orally or *intravenously* in doses of 50 cc of 10 per cent sodium iodide

5 Diphtheria antitoxin 5000 units intramuscularly immediately and repeated *in two days*

6 *Thiamine chloride 10 000 units intr imuscularly* daily Recently results that warrant further trial of this form of therapy were obtained by the injection of 1 cc of thiamine (100 mg per cc) and 1 cc neostigminemethyl sulfate (1 2000)

7 *Neoarsphenamine* 0 3 to 0 45 Gm (4½ to 6¾ grains) intravenously at four day intervals for four doses

8 Sodium salicylate and sodium bicarbonate equal parts *of*

each 1 33 Gm (20 grains) every four hours until 8 Gm (120 grains) have been given

9 Locally affected areas may be covered with a salve of equal parts of lanolin and petrolatum with one per cent procaine or 0 5 per cent cocaine and be protected by a silk dressing Calamine lotion with one per cent phenol or anesthetic dusting powders applied locally

10 Blocking appropriate sympathetic ganglions with procaine hydrochloride may give complete and lasting relief from pain The procaine block produces a temporary chemical paralysis and interrupts the cycle of nervous impulses

11 Deep x ray irradiation of the spinal cord and nerve roots or of the gasserian ganglion This form of therapy is of little value in the acute stage or if the condition has become chronic but may be initiated three weeks or a month after onset

ACUTE NEURITIS

Acute neuritis includes those lesions of the peripheral nerves which are due to inflammatory toxic or progressive degenerative processes

Etiology Many causative agents are known to produce neuritis The most salient of these are (1) Metabolic deficiencies as diabetes which in turn predisposes to arteriosclerosis (2) deficiency states as the various types of vitamin deficiency seen in beri beri pellagra or chronic alcoholism (3) infections as a primary process as in acute infectious polyneuritis or as a secondary complication of severe septicemia for example diphtheria and (4) poisons the chief offenders being lead arsenic and alcohol

Pathology Pathology varies with the etiological agent and therefore there may be few if any changes elicited in one case while marked damage is revealed in others In the latter there is usually a degeneration of the myelin sheath with proliferation of the sheath cells In addition the interstitial connective tissue may show inflammatory and proliferative changes In very severe cases the axon of the nerve cell may be completely destroyed

Signs and Symptoms The clinical picture depends on (1) Whether the process involves one or more peripheral nerves (2) the etiological agent and (3) the duration of the disease prior to seeing

the physician The constitutional symptoms are usually manifestations of the etiological agent The neuritic complaints are characterized by pain diminution of peripheral sensation and impairment of muscular strength along the distribution of the affected nerve The pain is usually sharp stabbing and radiates along the course of the nerve trunk Neuritic pains especially those in older patients having arteriosclerosis or diabetes or both tend to recur at nighttime

Paresthesias are common and hyperesthesia is elicited upon deep pressure over the involved nerve In mild cases only slight weakness may be noted but in severe and protracted cases there may be partial or complete loss of muscular power Deep sensibility may be partially or completely lost Reflexes likewise may be greatly impaired and at times absent If the case is untreated marked muscular atrophy and contractures may develop The cutaneous structures supplied by the affected nerve may also show evidence of inflammatory or degenerative change This is manifested by an increased redness scaling and sometimes necrosis of the epithelium

Prognosis Prognosis again depends upon the causative factor and the duration of the disease For example the neuritic process secondary to arteriosclerosis in the diabetic offers a poor prognosis In contrast the neuritic process seen in vitamin deficiency states and that secondary to acute infections offers a good outlook

TREATMENT

Treatment for the most part is supportive but the following points are deemed important in the management of the ailment

1 The etiological agent must be removed

2 Absolute bed rest is imperative

3 A high caloric and high vitamin diet should be given

4 Heat as hot as it can be borne with due caution to avoid burning where anesthesia exists should be applied Heat not only provides relief but usually hastens recovery and may be employed for several hours daily moist heat seems to be preferable to dry heat Physiotherapeutic measures as passive exercise massage short wave and ultraviolet should be instituted when the acute phase has passed

5 Massive doses of vitamin B_1 6 to 10 mg (1/10 to 1/6 grain) orally and 10 000 units intramuscularly should be administered daily

B_1 may also be given intravenously as one ampule containing 10 mg daily

6 Pain may be relieved with analgesics as sodium salicylate 1 33 Gm (20 grains) with sodium bicarbonate 1 33 Gm (20 grains) four times a day If not tolerated orally larger doses of the salicylates may be given rectally in starch retention enemas As much as 5 Gm (75 grains) may be given twice a day In the neuritides due to poisoning with metals especially arsenic the intravenous administration of sodium hyposulfite in doses of 1 Gm (15 grains) daily may be helpful Strychnine sulfate beginning with doses of 0 002 Gm (1/30 grain) and gradually increasing the dose to 0 006 Gm (1/10 grain) may be administered three times a day Potassium iodide 0 65 Gm (10 grains) three times a day each alternate week may be an aid in the elimination of metallic poisons

7 Ointments should be applied locally methyl salicylate ointment U S P commonly gives relief

8 The patient s general condition may be improved by intragluteal injections of liver extract 2 to 3 cc weekly and the administration of iron in the form of iron and ammonium citrate 1 33 Gm (20 grains) three times a day

9 Injection of the nerve trunk with 20 to 50 cc of two per cent novocain solution or 2 to 5 cc of alcohol may be resorted to in severe cases

CONVULSIONS

A convulsion is a symptom of a basic cerebral disorder which may be due to one or to several causes

Etiology A simple classification of the cause of convulsions includes

1 Cerebral
   a Trauma leading to skull fracture subdural hematoma or extradural clots
   b Tumors of the brain
   c Meningeal irritations as tuberculous meningitis or other forms of meningitis
   d Vascular diseases of the brain hemorrhage thrombosis or embolism
2 Toxic conditions
   a Acute alcoholism Convulsions may be caused by brain edema Lumbar puncture intravenous hypertonic solutions and sedation are necessary
   b Drug poisoning as strychnine

3 Constitutional diseases
  a Uremia The convulsion is associated with hypertension increased cerebrospinal fluid pressure and certain evidences of kidney disease
  b Hypoglycemia An overdose of insulin is usually the cause but it may occur in a patient who has a tumor in the islands of Langerhans Administration of glucose intravenously is the proper treatment until the complete diagnosis is established
  c Hypoparathyroidism
  d Pheochromocytomas of the adrenals with paroxysmal hypertension
  e Epilepsy
4 Cardiocirculatory diseases Stokes Adams disease—The patient has heart block The attack usually comes on suddenly and the patient falls as in an epileptic fit The administration of 1 cc of 1 1000 adrenalin intramuscularly or subcutaneously is usually effective in relieving the attack Between spells thyroid 30 mg (½ grain) three times a day and ephedrine 46 mg (¾ grain) two or three times a day may be given
5 Hysteria The convulsion may simulate an epileptic fit Other identification marks of hysteria are usually present to confirm the diagnosis

Signs and Symptoms Generalized convulsions are nearly always associated with loss of consciousness though there are a few exceptions as in strychnine poisoning the early stages of tetanus and so called jacksonian epilepsy *In strychnine poisoning the convulsion* is precipitated by such stimulants as loud noises or flashes of light Convulsions occur in spasms lasting one half to one and one half minutes often with relaxation between attacks In the early stages of tetanus the jaws are set the neck is stiff the abdomen is rigid and usually there is a history or evidence of some recent external injury Serum must be given and it is emphasized that 10 000 units given at the time of injury is worth more than a greater amount administered after symptoms of tetanus have set in In the so called jacksonian epilepsy convulsions are limited to one part or one side of the body This condition is due to diseases confined to the cortex of the brain

Complete loss of consciousness is the general rule with the exception of the instances mentioned above Both sides of the body face arms and legs are equally involved though sometimes the attacks are unilateral at first and bilateral later Convulsions usually commence in the same way that is at first there is a tonic spasm followed by clonic convulsions and then there is a period of coma Usually *convulsions* last for a minute or a few minutes and return at uncertain periods later on sometimes one convulsion follows another so

rapidly that there is no breathing spell between them and the patient dies of exhaustion respiratory paralysis or heart failure

Diagnosis There is no difficulty found in differentiating the type of convulsion present However there are several laboratory aids especially for convulsions caused by hypoglycemia to which every suspected case is entitled These include a sugar tolerance test an epinephrine test and an insulin test

Prognosis The convulsions of adults are generally of greater seriousness than those of infants since the underlying organic disease is very likely to be of more importance A convulsion itself is not so dangerous but the underlying disease that accounts for it is always a grave matter

TREATMENT

A convulsion is a symptom of some underlying disease and therefore the treatment must be divided into two stages the immediate and the after treatment

1 The immediate treatment is important because a convulsion is always an emergency and may lead to respiratory failure cardiac exhaustion and death Regardless of the cause measures must be instituted immediately to control the episode

a Phenobarbital orally or sodium phenobarbital in adequate dosage until convulsions cease may be given and then continued for 6 hours every 2 days If this drug is not effective tribromethanol (avertin) in doses of 75 mg per kilogram by rectum may be given Also of use is ether or chloroform inhalations to the point of depression If *sodium amytal is given 0 24 to 0 46 Gm (4 to 7 grains) it must be* administered intravenously

b Some article like a tongue depressor or a wooden stick wrapped with gauze should be inserted between the teeth so the tongue will not be cut.

c If the irritant has been taken orally the stomach should be washed out with 1 1000 potassium permanganate solution and then chloral hydrate and sodium bromide 1 33 Gm (20 grains) *of each should be* given by rectum or mouth.

d Sedatives as morphine sulfate 0 016 Gm (¼ grain) or pantopon 0 02 Gm (⅓ grain) hypodermically may be administered to control mild convulsive states

e If during the convulsive seizure respiratory depression becomes so great that the patient stops breathing and turns blue an immediate injection of some stimulant as caffeine *sodium* benzoate 0 33 Gm.

(5 grains) coramine 2 to 4 cc (1/ to 1 dram) or strychnine 0 002 Gm (1/30 grain) hypodermically must be given to preserve life

f In order to control repeated convulsions the patient should be removed to a quiet dark room where the treatment of the immediate emergency may be continued

g Edema of the brain may be an important feature in such diseases as chronic alcoholism uremia lipoid nephrosis and acute elevation of chronic hypertension Removal of spinal fluid is helpful but caution must be exercised Spinal puncture should be done only after grave consideration is given to the possibility of a brain tumor and to the ill consequences of such an action if a tumor is present Hypertonic glucose or sucrose 100 to 300 cc of 50 per cent solution may be given intravenously but sucrose should be avoided in the presence of anuria

h In uremia of the convulsive form there may or may not be edema An elevated blood pressure is more significant than any other sign and is probably the remote cause of the convulsion Magnesium sul fate 10 cc of a 25 per cent solution may be given intravenously or intramuscularly and repeated every four hours Results are often remarkable

2 The after treatment of a convulsion requires that the under lying cause be uncovered and the condition whether organic or func tional be remedied Whenever possible a urinalysis blood sugar determination and simple blood count should be done because fre quently the cause of the convulsion lies in a common disorder revealed by such routine tests

MIGRAINE

Migraine is a symptom complex dependent on unknown factors It is generally applied to a severe paroxysmal headache affecting only one side of the head Such headaches are generally preceded by mild aura associated with vomiting and terminated by sleep There are however headaches classed as migraine which do not present all these symptoms

Etiology Migraine occurs more frequently in women than men with a ratio of about 2 5 to 1 It begins early in life often at puberty is recurrent and tends to disappear during pregnancy and after the menopause The malady often runs in families and may be heredi tary Infectious diseases as influenza malaria syphilis gastrointes tinal disturbances chill anemia fatigue prolonged nervous strain or mental exhaustion have all been considered as causes There is

considerable evidence that the endocrines the pituitary gland in particular have some relation to the disease

The most plausible explanation to date is that migraine is caused by a vascular spasm due to vasomotor disturbances Oppenheim s belief that the cause is disturbance of the sympathetic innervation may be correct though the underlying factors are as yet unknown The vascular storm is said to produce localized edema in the occipital cortex resulting in visual phenomena and increased intraventricular pressure producing headache and vomiting

Foods may be a contributory factor as migraine is often found in persons who are allergic

Signs and Symptoms Migraine is a periodical or paroxysmal headache with gastric disturbances The attack is preceded by a feeling of pressure in the head dullness moodiness yawning somnolence dizziness and occasionally by nausea anorexia or choking sensations The headache is as a rule unilateral but may be frontal temporal parietal or occipital It is at first dull but grows in *intensity until it is almost unbearable at times causing the patient* to cry out in pain At the height of the attack there is apt to be vomiting Migraine headache terminates in sleep

The headache is often preceded by visual disturbances such as spots before the eyes contracted visual field blind spots or scotomas There may also be disturbances of sensation speech or motility

Pallor or redness of the face dilatation of the pupils or salivation may appear as a result of migraine The disorder resembles epilepsy when it is accompanied by symptoms such as tics cramps or convulsions Abdominal pain and gastric hypersecretion have been reported in connection with migraine

Diagnosis Migraine headache is usually easy to recognize In atypical cases however there may be diagnostic difficulty The diagnosis should not be made too often Organic disease of the brain tumor or aneurysm of the cerebral vessels syphilis epilepsy uremic and arteriosclerotic headache sphenopalatine neuralgia headaches due to eye conditions or infections of the sinuses should all be ruled out before *a diagnosis of migraine is made*

Prognosis Migraine headache may last from several hours to a day or more In neurotics the hemicrania may become constant Migraine may last part or all of one s life though it usually stops

at the menopause or during pregnancy Prognosis is unfavorable as to cure but favorable as to life The ophthalmoplegic type is more serious as are migraine headaches associated with hysteria

TREATMENT

The treatment for migraine is not entirely satisfactory However the following drugs have been used in therapy

1 Macy and Horton have recently reported the use of histamine in a series of migrainous patients The initial subcutaneous dose was 0 1 cc of a solution containing 0 275 mg of histamine phosphate per cc Succeeding doses were increased by 0 05 cc of the solution If given *intravenously 0 1 to 1 mg of histamine* was administered The intravenous route was not as satisfactory as subcutaneous administration Sometimes however flushing of the face headaches nausea and vomiting develop making it necessary to stop these injections temporarily resuming treatment with increments being made more slowly

2 Ergotamine tartrate if given early may abort the attack It should be given in a dose of 0 25 mg (1/240 grain) subcutaneously and repeated *in 2 to 3 hours if necessary* Dihydroergotamine (D H E 45) has largely replaced ergotamine and may be administered in doses of 1 25 to 1 5 cc intramuscularly in about 1½ hours

3 In some cases oxygen breathing for an hour or two or a rectal suppository of 0 2 Gm (3 grains) of nembutal will stop nausea and vomiting In severe cases of nausea and vomiting sodium amytal 0 24 to 0 47 Gm (3¾ to 7¼ grains) intramuscularly has proved beneficial

4 E E Hines of the Mayo Clinic at Rochester Minnesota advocates the use of potassium thiocyanate in 0 2 Gm (3 grain) doses three times daily in patients with migraine associated with *hypertension The blood level of 10 to 12 mg* of cyanate per 100 cc per cent of blood is considered optimal It is suggested further that this treatment is to be used in combination with estrogenic therapy in women whose headaches are aggravated around the time of menstruation In this case progesterone 5 to 15 mg has been said to bring relief

5 The use of methyl iso octenylamine (octin) 2 grains (1 tablet) orally and repeated every half hour if the headache is not

relieved or until 4 tablets have been taken or 0 5 cc (1½ grains per cc) intramuscularly has been said to bring symptomatic relief in some types of migraine Phenacetin antipyrine amidopyrine or aspirin may give relief Amyl nitrite pearls or nitroglycerin sometimes overcome vasomotor spasms Codeine or morphine can stop the attack but the danger of addiction is too great Pituitary gland extract 0 06 Gm (1 grain) alone or in combination with 0 016 Gm (¼ grain) of thyroid may be used if there is a suspicion that the pituitary gland is involved Phenobarbital is sometimes good

6 Cold compresses to the head and hot foot baths are traditional measures If anemia is present it should be treated with iron arsenic or other acceptable therapy

7 Prophylactic measures such as avoidance of excessive worry and excitement careful attention to the diet and at times the use of small doses of sedatives may be of aid Focal infections should be attended to visual defects corrected and gastrointestinal disorders looked after

HEAT EXHAUSTION AND SUNSTROKE

Heat exhaustion is a state of weakness dizziness pallor and profuse perspiration resulting from exposure to high temperatures over a prolonged period of time Sunstroke (heatstroke) is a disturbance of the heat regulating mechanism of the body due to the same pathogenesis

Etiology The etiology in both conditions is exposure to extreme degrees of heat usually over a long or relatively long period of time Association of the extreme heat with high humidity is particularly important in the causation of these states

The pathology is not distinctive Cerebral and visceral congestion are the chief changes and if death is sudden there may be no noteworthy lesions

Signs and Symptoms Heat exhaustion is distinguished by weakness dizziness pallor and cold clammy sweating Stupor and rarely loss of consciousness are seen Pulse and respiration rates are accelerated and the blood pressure is lowered The oral temperature may be subnormal or very slightly elevated The rectal temperature however is alleged by tropical experience to be invariably raised to about 38 3° C (101° F) The onset is usually sudden and is not

always precipitated by exertion Where the environment is one of sustained heat there may be a prodromal period of several days of malaise headache, anorexia and constipation

Frequently there is no clear line of demarcation between heat exhaustion and heatstroke and cases of heat exhaustion may after a time reveal evidence of sunstroke The onset of the latter may occur with overwhelming suddenness and death may follow shortly Premonitory cephalalgia dizziness nausea or visual disturbances may precede the prostration Consciousness is lost early The face is flushed and the skin dry and hot The temperature rises at times to 43 3° C (110° F) or higher In the early stages the pulse is full and rapid and the breathing is deep as the condition advances the pulse grows irregular and feeble and the respirations more shallow and of Cheyne Stokes variety at times

Heat cramps are another manifestation of prolonged heat exposure due to a concomitant depletion of blood chlorides The condition *is found particularly among stokers miners and steel workers* The onset is sudden Cramps involve the muscles of the extremities or of the abdominal wall They may occur intermittently for 24 hours and rarely longer

Prognosis The death rate from heat in the United States for the period from 1900 to 1932 amounted to 0 39 per 100 000 *Deaths* from heat are closely correlated with unusually high atmospheric temperatures continuing for several days and are commoner in men than in women Death from sunstroke may occur within a few minutes but if the patient survives the second day recovery is probable Persistent susceptibility to heat and impairment of memory are noticed after attacks of heat exhaustion and stroke

TREATMENT

1 The patient with heat exhaustion should be brought to lie in a cool place

a Clothing should be loosened and water given by mouth

b Mild stimulants as aromatic spirits of ammonia 2 to 4 cc (½ to 1 dram) in a glass of water should be given orally if the pulse continues to be rapid and weak.

c If the situation is one where the temperature falls well below normal external heat must be administered and hot drinks given Here caution

must be exercised to prevent the passing of the condition into sunstroke

2 The important and essential treatment of sunstroke is to reduce the body temperature to a tolerable level

a The patient may be placed in a bath of water cooled to 10 C (50 F) and kept there until the rectal temperature falls to around 39 C (102 F) After this level is reached the body in favorable cases will continue to lose heat even after being removed from the water

b The skin must be massaged continuously while the patient is in the tub otherwise the overheated blood may be driven inward by peripheral vasoconstriction

c An ice water enema 1000 cc or more should be given

d The body may be rubbed with ice or placed in sheets wrung out of ice water

e Water may be sprayed onto the stripped body from a fine nozzle and accompanied by a current of air from hand or electric fans

3 The victim of heat cramps must also be removed to a cool place

a Frequently rest alone is followed by subsidence of the cramps

b Sodium chloride 1 Gm (15 grains) every hour should be given until 15 doses have been administered It may be injected intravenously if necessary

4 Preventive Treatment The untoward effects of heat are frequently due in part not only to the excessively high temperature of the environment and to chloride depletion but to excessive heat production by the body and to insufficient production of sweat Diet and clothing should therefore be adjusted to the environment

a Soft fine clothing or little or no clothing should be worn so greater amounts of sweat may be produced and absorbed or evaporated

b The diet should be bland and easily digestible consisting of light fruits and vegetables rather than of calorie producing meats and fats

c People in industry who work in high temperatures require more than the average amount of salt and may obtain it by adding one level teaspoonful to each quart of water or by taking one 15-grain tablet of sodium chloride with every glass or two of water

CAROTID SINUS SYNDROME

Hyperactivity of the carotid sinus reflex is strictly a clinical syndrome which may occur in association with a variety of diseases

It is characterized clinically by episodes of fainting dizziness with or without convulsions and usually a decided arterial hypotension

Etiology This syndrome is often found in association with coronary heart disease and whenever the disorder is recognized a careful study of the cardiac mechanism should follow However there are other conditions such as cerebral vasoconstriction which if not the cause of the carotid sinus syndrome are associated with it An unstable vasomotor system is usually present There is no unanimity of opinion at present concerning the exact etiology of the hyperactive carotid sinus syndrome

Pathology As this is a functional disorder pathological changes in the tissues are not described

Signs and Symptoms Fainting vertigo visual disturbances general weakness buzzing in the ears and numbness and tingling in the extremities are the characteristic symptoms These come on at irregular intervals and are usually precipitated by constriction of the neck as occurs with tight collars psychic trauma emotional disturbances and upsets and by continued fatigue

Patients appear to be in good health and no evidence of mal nutrition is noticed Pallor a tendency to clammy skin lightheadedness and lack of the usual physical energy are features Two types of this syndrome may be recognized Clinically one is associated with marked hypotension with other evidences of vasodilatation and a slow weak heartbeat The other form is distinguished by a blood pressure which does not fall to abnormal levels but the bradycardia is present

Diagnosis Confusion may occur in the diagnosis of the carotid sinus syndrome with such diseases as epilepsy early Addison s disease coronary disease of the heart early tumors of the brain hysteria Stokes Adams disease and chronic hemorrhagic pachymeningitis interna The diagnosis of hyperactive carotid sinus reflex is made by applying pressure with the thumb over the carotid artery where the common artery bifurcates and forms the internal and external branches Pressure over this area will be exerted on the sinus In the presence of the disease pressure on one side or the other usually causes slowing of the heart pallor weakness convulsions and as a rule a marked drop in arterial blood pressure

Prognosis *The immediate prognosis concerning life is good* The

disorder may persist for several years and then disappear and never return again Sometimes it becomes such a serious problem that drastic measures such as resection of the carotid sinus nerve are necessary

TREATMENT

1 All existing associated abnormalities should be corrected if possible Emotional upsets or other conditions which might precipitate an attack should be eliminated

2 One milligram (1/60 grain) atropine sulfate orally three or four times a day or tincture of belladonna 1 cc (15 minims) t i d will usually prevent attacks the least amount of the drug necessary to prevent attacks should be given If there are distressing effects from the drug 30 mg (1/2 grain) ephedrine sulfate should be given orally three times a day instead of atropine Phenobarbital 15 mg (1/4 grain) may be given in conjunction with these drugs if there is excessive nervousness or palpitation of the heart Thyroid 60 mg (1 grain) b i d may do good

3 According to some authors roentgen therapy may be of prophylactic value over a considerable period of time

4 If medication fails to relieve this condition neurosurgeons may bring about relief by resecting unilaterally the carotid sinus

SUBARACHNOID HEMORRHAGE

Subarachnoid hemorrhage is bleeding into the subarachnoid space from trauma and other causes

Etiology While there are undetermined causes of this condition the known causes of subarachnoid hemorrhage are trauma intraventricular or massive cerebral hemorrhage blood dyscrasias ruptured intracranial aneurysm septic or infectious embolism arteriosclerotic degeneration of vessel walls and ruptured cerebral neoplasm It may occasionally result from shock therapy

Pathology Traumatic subarachnoid hemorrhage usually occurs in all lacerations of the brain causing blood to appear in the spinal fluid which irritates the cells of the arachnoid and causes blockage of the arachnoid villi where cerebrospinal fluid is absorbed into the venous blood sinuses

In spontaneous hemorrhage the common lesion found is atheroma of the cerebral vessels or the arteries at the base of the brain

Signs and Symptoms The onset is sudden usually after physical exertion or excitement Headache *vomiting and dizziness are the* initiating symptoms caused by the blood escaping into the subarachnoid space and increasing the intracranial pressure The blood then travels along the sheaths of the optical and cranial nerves This may result in increased intraocular pressure retinal hemorrhages, pupillary changes from day to day, hyperemia of the disks facial paresis and deviation extraocular palsies ringing in the ears and respiratory and cardiac disturbances Nuchal rigidity is common A mild Kernig sign may be present Usually the consciousness of the patient is impaired in varying degrees

Mild leukocytosis elevation of temperature and slow pulse compared to the temperature are generally characteristic

Diagnosis The spinal fluid is uniformly bloody but varies in intensity of color On standing the red blood cells collect at the bottom of the test tube while the top fluid is yellow or orange

Subarachnoid hemorrhage may simulate septic meningitis encephalitis tumor of the brain uremia or sinusitis

Prognosis Recovery from the initial attack has been reported as being approximately 50 per cent Unfavorable factors as regards prognosis are history of previous attacks multiple hemorrhages mental disturbances *unconsciousness and convulsion*

TREATMENT

1 The headache should be relieved immediately by the administration of mild sedatives as codeine and acetylsalicylic acid The head of the bed may be elevated

2 The intracranial pressure may be reduced by hypertonic dextrose *or sucrose solutions intramuscular injections of magnesium* sulfate or caffeine with sodium benzoate Lumbar puncture should be exercised with care being used only in those cases due to trauma arteriosclerosis or unknown causes or to arrive at a diagnosis In other cases repeated punctures may cause the patient s death Usually only 5 to 10 cc should be withdrawn at any one time It may be said that dramatic results in relieving the patient s symptoms have occurred in cases which refused to react to other medications

3 An adequate amount of nutritious food should be given Since many of these patients have no appetite vomit or are uncon

scious tube feeding may have to be resorted to Fluid intake should be limited to 1200 cc per day Salt and vitamins should be given

4 Paraldehyde intramuscularly by mouth or rectum will reduce excitement or a mild restraint may be employed

5 Patients should be kept in bed for six weeks and allowed to convalesce for six months It is important to protect the patient from excitement and physical exertion of any kind

CHAPTER XII

The Kidneys

ACUTE NEPHRITIS

Acute nephritis may be subdivided into acute glomerular or hemorrhagic acute tubular and acute interstitial It is the acute glomerular form which is usually encountered and it is the one given most consideration in this chapter The acute tubular disease is the result of toxic substances such as mercury and the sulfonamides which involve the tubular apparatus almost exclusively Acute interstitial nephritis follows acute infections as measles and diphtheria Since both the tubules and the glomeruli usually are involved when the kidney is caught in an inflammatory process it is not practical for the present purposes to consider them separately

According to onset and course acute diffuse glomerular nephritis may be divided into the insidious type in which the classical textbook picture is lacking and the type characterized by an abrupt onset in which albuminuria hypertension hematuria and edema are the clinical symptoms In the first form the immediate prognosis is usually quite good but in the latter type acute heart failure convulsions or uremia may be fatal in the early stage

Etiology and Pathology Acute infections practically always precede the onset of acute nephritis and nearly all writers are unanimous in the opinion that upper respiratory infections constitute the chief cause Diphtheria measles chickenpox suppurative lymph glands chills appendiceal abscess or almost any infection in the body may be *responsible* for *nephritis* but *tonsillitis septic* sore throat and otitis media are the main predisposing diseases

Pathologically acute glomerular nephritis is not merely a disease of the kidney but may involve various systems of the body as well as the glomerular tufts The term is used because the capillaries of the glomeruli are practically always the site of the initial lesion While it is known that infection by streptococci plays the predominant role in the cause of acute glomerular nephritis the mechanism by which

glomerular inflammation arises is not entirely clear It is almost universally accepted that the streptococci do not cause glomerular inflammation by direct invasion The most widely held opinion but one that lacks positive proof is that the streptococci call for the production of antibodies in such concentrations that an interaction develops between the formed antibodies and the antigen itself resulting in the formation of a toxic material which is responsible for the injury of the capillaries of the glomeruli It has always seemed rather paradoxical however that Nature in its wise provision for warding off the attack of the streptococci adequately would thereby subject essential organs of the body to such a crippling disease as glomerular nephritis

The chief changes occurring in acute glomerular nephritis are swelling and disintegration of the endothelial cells which line the capillaries of the tufts The process is a diffuse one involving all glomeruli in all the tufts some glomeruli are more severely involved than others but practically no glomerulus escapes some injury The tubules in the very early stages of acute nephritis may remain intact but in a few days cloudy swelling granular degeneration and disintegration of the epithelial cells commences The proximal and distal types are especially involved Grossly the kidney is large and ischemic and the capsule is usually under greater than normal tension so that when the capsule is nicked it splits away from the kidney parenchyma by virtue of the intracapsulary tension Microscopically the glomerular loops are practically bloodless since the swollen epithelium occludes the lumen of the capillary The degree of inflammatory change noted under the microscope varies considerably with the intensity of the inflammation However the clinical features may be easily explained by the pathologic changes in the kidney and correlation between the changes in the glomeruli and the tubules and the clinical picture is usually discernible

Signs and Symptoms *Following an acute infection* for example an upper respiratory infection the patient may develop the clinical picture of acute nephritis within a period of from two to eight days The classical textbook picture of hematuria hypertension edema and nitrogen retention is not always present more often the patient has only evidences of renal inflammation as shown by the urine examination Albuminuria red blood cells pus cells and casts in the

urine are frequently the only signs and are often overlooked if symptoms are absent

It must be realized that in the kind of acute nephritis which sets in abruptly death may occur within the first week The patient must be protected from acute heart failure convulsions with death renal failure and acute genuine uremia The onset of heart failure may be the first evidence of nephritis for sometimes it shrouds the clinical picture of renal disease Proper treatment of the acute phase in this kind of acute nephritis requires prompt and drastic measures as the disorder is analogous to the acute abdomen in surgery Prompt recognition immediate treatment and careful and continuous watching are needed to save the lives of these patients

In dealing with acute nephritis however there are several syndromes which must be considered all of these syndromes need not be present at the same time one may develop and dominate the clinical picture for a time and then disappear temporarily or permanently

The urinary syndrome is the one of greatest importance because most reliance can be placed on the urinary changes Disturbances of urination characterized by a scanty outflow of urine or even complete anuria may be present In these cases examination always reveals red blood cells pus cells and casts in the urine Many times the oliguria is not marked enough to be recognized unless it is looked for specifically The severity or mildness of the kidney disease cannot always be measured by the examination of the urine or any other tests

Hypertension is present in about 40 per cent of cases of acute nephritis It is not an obligatory sign as it was thought to be years ago yet the onset of hypertension in acute nephritis is always a serious and frequently a disastrous complication If it is present at the beginning and drops to normal within the first week or two of the disease when resolution begins to set in less importance is attached to it If on the other hand the blood pressure appears and continues to rise gradually after the renal disease is in progress this is an unfavorable prognostic sign Associated with hypertension may be such clinical findings as headache visual disturbances vomiting convulsions and loss of consciousness These complications were at one time thought to be the result of edema of the brain and al

though edema of the brain may be present it is the hypertension that is behind these features

At times the blood pressure rises rapidly to 200/120 mm of mercury and a distinctive clinical feature found at this time which may develop within a period of 12 hours is the so called albuminuric retinitis As the eyeground is looked upon as a mirror of changes in the kidney this kind of examination is of utmost importance Ophthalmoscopically the retina is seen to be pale and the arteries thin and almost bloodless The margins of the disks are often blurred with later development of genuine choked disks and within a short time hemorrhages may be seen throughout the retina associated with fresh white fluffy patches

Edema is the syndrome which gives most concern to the laity but to the physician it is probably of least importance unless it makes its first appearance after the disease is in progress for a week or two At this time it indicates an extensive involvement of the kidney frequently a permanent one Edema gives the patient a bloated appearance around the eyes and a roundness and fullness to the face contributing to the characteristic pallor which is frequently an early feature of acute nephritis

Like edema azotemia in the early periods of acute nephritis is of little significance but when it occurs after the first ten days its presence causes concern because it indicates that the functional capacity of the kidney is reduced While the initial rise in nonprotein nitrogen in the acute episode is not of great importance it does point out to the physician that he must establish urinary flow as soon as possible As a rule if this condition is allowed to go uncorrected for seven or eight days genuine fatal uremia sets in

Clinically after the first two weeks of acute nephritis some patients completely recover from the disease at times however the recovery is more apparent than real After the acute episode a latent period may follow in which the patient may feel well but upon careful examination of the urine one may find albumin an excessive number of red blood cells white blood cells and granular casts indicating an inflammatory kidney lesion

Sometimes these latent cases go on to recovery while others continue and finally terminate with chronic glomerular nephritis Per

haps the greatest problem in the management of acute nephritis is to recognize this latent stage and to deal with it satisfactorily

Differential Diagnosis At times there may be difficulty in distinguishing between genuine acute nephritis and an acute exacerbation of chronic nephritis The question of a differential diagnosis is an involved one however, it is felt that in the chronic form of the disease the blood pressure is more likely to be increased and the heart markedly enlarged without symptoms of myocardial insufficiency than in the acute form

Prognosis General opinion as to the prognosis of acute nephritis in the early stages is particularly good and it is estimated that only 3 to 6 per cent of patients die during the acute stage Follow up studies over a period of years however show a disparity of belief as to prognosis

TREATMENT

The chief aim in the treatment of acute nephritis is to prevent further deterioration of the inflamed kidney and at the same time to maintain as well as possible the general health of the body This is accomplished by using measures which not only are directed at curing the disease of the kidney but restoring the physiological functions of the body which have deviated from normal

Treatment consists in shielding the patient from acute infections as much as possible and protecting the kidneys when the patient actually develops acute infection It seems that this has been quite satisfactory in scarlet fever but not so effective in cases of simple upper respiratory infection Complete rest alkalinization and regulation of food intake are the chief safeguards in this phase The following is a summary of treatment

1 The patient must be kept in bed until all signs of renal inflammation have passed This means more than keeping the patient in bed while hypertension edema and hematuria exist The patient must remain in bed as long as the microscopic examination of the urine shows red cells casts and albumin and until the sedimentation rate becomes normal Other tests helpful in the detection of unhealed renal lesions are the concentration test and blood urea clearance test The presence of an unresponsive anemia indicates that the kidney damage is becoming worse It is generally well to insist on four months of modified bed rest If the kidney has not

cleared up by this time the condition is probably chronic and continued rest will have no effect

2 In order to restore the body functions to normal one must first know the disturbances which have resulted from renal insufficiency This requires a fundamental knowledge of the water balance salt and alkali reserve the plasma protein content and the amount of nitrogenous substances retained in the blood To achieve good results one should give 2000 to 3000 cc of fluid daily in the form of fruit juices milk imperial drink or water When there is vomiting the same quantity may be given intravenously A physician is often in doubt as to what kind of fluid to administer to the patient In general 1000 cc of 10 per cent glucose solution may be given slowly intravenously once or twice a day depending on the needs of the individual If there is acidosis or a rapidly rising nonprotein nitrogen 1000 cc of 1/6 molar solution of sodium lactate may be prescribed in addition One thousand cc of normal saline solution may also be added if renal insufficiency is associated with a depletion of sodium chloride from the blood Fifty cc of 50 per cent glucose solution intravenously with 0 5 Gm (8 grains) of aminophylline may also be given

3 *The diet requires special consideration* The optimal quantities of protein salt and fluids vary so much with the requirements of each case that it is difficult to lay down precise instructions However the following generalizations may be helpful

Protein increases the work of the kidney and may augment the inflammation and retard the healing processes Usually 1 to 2 Gm per kilo of body weight are sufficient to meet the body requirements If there is a deficiency of protein in the diet the kidney may be spared but the patient suffers as a consequence Sometimes plasma proteins especially albumin are greatly reduced and play a role in edema formation Then it is wise to give more protein to make up the deficiency Albumin may be given intravenously in amounts varying from 12 to 25 Gm every day for three days until plasma albumin rises Amino acid therapy has been used to induce a positive nitrogen balance and as a means of improving serum albumin levels but it is unpalatable and has a relatively high sodium content Acacia gelatin and globin have also been used to bring up the colloidal osmotic pressure

Rarely is there ever a sodium chloride deficiency in acute nephritis but an excess of salt in the body is common A diet low in *sodium chloride is given to prevent* edema *This is satisfactorily* accomplished by withholding the addition of salt from food It is seldom necessary to resort to rendering natural foods salt free It is wise to watch carefully the sodium and chloride content of the blood in nephritis for in the presence of renal insufficiency a depletion of sodium chloride may occur This can be rectified by the addition of 2 to 3 Gm (30 to 45 grains) of salt daily by mouth or by giving *500* cc of normal saline solution intravenously daily for two or three days

4 *Sulfonamides may be beneficial in the treatment* of nephritis Williams Longcope, and Janeway used sulfanilamide and noted that it increased the incidence of recovery and prevented progression of the condition I have seen good results follow the use of sodium sulfathiazole and sodium sulfadiazine Of course this form of treatment must be used with caution as severe renal damage may ensue either as a result of obstruction due to clumps of crystals in the *tubules pelves or ureters or as a result of direct nephrotoxic* action As a rule untoward reactions may be avoided if a few simple precautions are taken The urinary output must also be closely checked with special emphasis on quantity and appearance on gross and microscopic examination If crystals are detected extra care must be exercised in regard to dosage blood level and urinary output Alkalinization of the urine may reduce the incidence of *crystalluria Experimentation shows that if the pH of* the urine can be kept well above 7 the occurrence of crystalluria is diminished The sulfonamides should not be given before any renal insufficiency or obstructive uropathies have been carefully evaluated

5 Resistance of the individual plays an important part in recovery and renal inflammation is less likely to subside in a person who is anemic and whose strength is sapped by the causal infection which *usually accompanies* the nephritis Vitamins play an important part in building up the resistance of the individual and should be given daily A and D may be given in the form of cod or halibut liver oil capsules B complex in brewer s yeast and supplemented by intramuscular injections of thiamin chloride 2 to 3 cc daily Vitamin C may be given in *tablet form The value of iron has been proved by*

careful observers and may be administered in the form of iron ammonium citrate 0 66 Gm (10 grains) three times daily Rutin may also be a valuable adjunct in therapy

6 If diuresis can be established the signs and symptoms of acute nephritis usually subside Water is the most important of all diuretics but simple diuretics as potassium citrate 1 33 Gm (20 grains) three or four times a day or a combination of potassium citrate and potassium acetate each 1 33 Gm (20 grains) three times a day in liquor ammonium acetate may be administered to aid in the promotion of diuresis Caffeine sodium benzoate 0 45 Gm (7 grains) twice a day or strophthanine 1/100 grain intravenously may be administered in cases of anuria partially accounted for by circulatory failure The stronger diuretics are to be condemned in the treatment of acute nephritis

7 In the course of acute nephritis the heart in certain cases may have to bear the brunt of the blow This is particularly true if hypertension is present In this case the heart becomes dilated and the apex beat shifts well to the left If convulsions set in the strain on the heart is accentuated and the patient may die of acute dilatation of the heart More familiar though is the patient with a slowly dilating left ventricle followed by pulmonary edema which gradually becomes worse until finally death comes from advanced pulmonary edema In these cases treatment is largely symptomatic The hypertension may be controlled by giving 3 Gm (45 grains) of magnesium sulfate dissolved in 120 cc of 5 per cent glucose solution twice a day or more often depending upon the blood pressure and general condition of the patient Venesection may also be employed with good results and sometimes digitalis in doses of 0 1 Gm (1½ grains) three times a day or digitoxin in doses of 0 2 mg daily orally or intramuscularly is beneficial Sedation may be given as required and at times oxygen promotes comfort

8 The complications pointing to cerebral involvement such as nausea vomiting visual disturbances headache and coma are familiar to every practitioner and are serious emergencies The treatment of these complications is as follows

a Of value is 50 cc of 50 per cent glucose intravenously and magnesium sulfate given in divided doses of 2 to 4 Gm depending upon the condition of the patient and the height of the blood pressure

b Sometimes spinal puncture is necessary in order to reduce the pressure of the spinal fluid

c Sodium amytal 0 2 Gm (3 grains) or some other sedative of light nature must be given to quiet the patient If convulsions are occurring the sedative should be administered intravenously Fifty cc of 50 per cent sucrose solution have been advocated but it is considered unwise to use the sucrose solution for cerebral complications unless there is a fairly good urinary output

UREMIA

Uremia is a clinical syndrome caused by retention in the blood and tissues of toxic substances which should have been excreted in the urine

Until 1870 when Traube stated that convulsive uremia was due to edema of the brain no differentiation was made between the different forms In 1912 Volhard and Fahr separated uremia into two great classes The nomenclature identifying these groups varies considerably but it may be stated that a patient either has (1) genuine uremia or (2) convulsive uremia

Etiology and Pathology Whenever the kidney s chief function of making urine is impaired uremia may be the result if so large a portion of the renal parenchyma is destroyed that the remainder is unable to compensate for it It is felt that the etiologic factor of this condition is toxic although the nature of the toxin is not known At autopsy uremia enteritis and pericarditis may be found and the alimentary canal may be affected Common findings in the lower part of the small intestine and the colon are necrotizing and ulcerative lesions

Signs and Symptoms As has been stated above uremia may be divided into two groups Genuine or convulsive

Genuine uremia is the direct outcome of renal insufficiency developing when the kidney fails to excrete urine and the toxic materials are retained in the blood stream It may be due to tuberculous destruction malignancy pyelonephritis or it may be the direct outcome of Bright s disease It is distinguished clinically by the following features

a There may be the cerebral type in which the patient is maniacal euphoric or stuporous In these cases the stupor gradually merges into renal coma

b The gastrointestinal type is that pointed out by Osler as the typhoid form There may be diarrhea tympanites vomiting dehydration and at times hematemesis

c The cardiorespiratory type is the form in which there is severe dyspnea usually without apparent cardiac disablement Uremic pericarditis develops in this form

Convulsive uremia stands out in direct contrast to genuine uremia since it is not dependent on renal failure and retention of nitrogen *has no connection with the condition It is distinguished* by high blood pressure associated with edema of the brain leading to convulsions If the diastolic pressure is above 120 or 130 edema of the disks is usually present and the spinal fluid pressure is usually greatly increased The convulsive attack simulates closely epileptic attacks after the convulsion there is a clonic convulsion followed by stupor

Diagnosis Without the laboratory aids a diagnosis of uremia *may be difficult since other conditions notably cerebrovascular dis* orders may simulate it However one may suspect the condition after a period of oliguria occurring in combination with a low specific gravity By determining the status of the blood urea or nonprotein nitrogen the diagnosis may be clinched

Prognosis The outlook varies with the patient Convulsive uremia frequently clears up and the patient lives for years in com *parative comfort* On the other hand *genuine uremia usually means* that the kidneys have failed and the chances of prolonging life are slight

TREATMENT

The treatment of uremia is not always attended by unsuccessful results It must be kept in mind that uremia may be produced by a variety of conditions Some of the diseases that may cause uremia *respond fairly well to treatment* as *hypertrophy* of the prostate obstructive lesions in the upper urinary tract which are removable and the uremia which comes on in the hypertensive arteriosclerotic individual who develops some myocardial insufficiency and extensive dehydration The uremia of the end stage of chronic glomerulo nephritis is usually irresponsive to any treatment and only temporary alleviation of symptoms can be anticipated

The most dramatic results in the treatment of uremia *often* are obtained in those cases where the uremic condition is caused by a

closing down of the kidney in the presence of dehydration and myocardial insufficiency In such cases it may appear from the examination that the kidneys reserves have all been lost, but administration of fluids and other treatment are frequently followed by a complete recovery from the uremia and by years of active existence even though the reserve forces of the kidney are below normal

While many therapeutic attempts have been made to control uremia most of them may be summarized in the following rules

1 By far the most important aid in genuine uremia is the administration of fairly large quantities of fluid Since the patient usually cannot take or retain very much liquid by mouth 2000 to 3000 cc a day should be given intravenously The output of the toxic products of metabolism is dependent largely on the output of urine therefore the urinary output becomes the problem of main concern Naturally the way to increase the output of urine is to increase the intake of fluid It is emphasized that a very accurate record of the intake of fluids must be kept to aid in the management of the patient with uremia

In convulsive uremia it is not wise to push fluids because dehydration is desired for the purpose of reducing the edema of the brain and the spinal fluid pressure There are times however when it is necessary to give fluids to increase the output of urine In these cases the fluids must be given slowly and cautiously Magnesium sulfate in 20 per cent solution in amounts of 10 to 20 cc intravenously two or three times daily has been used to control the convulsions which may occur Dextrose 50 to 300 cc of 30 per cent solution may be given instead of magnesium sulfate I have used sucrose 300 cc of 50 per cent solution intravenously to reduce the spinal fluid pressure and edema of the brain It not only promotes diuresis in a way that cannot be accomplished by other solutions but the patients seem much improved clinically after these sucrose injections

The kind and quantity of fluid to be used are not always easy to determine The rational procedure is based on a consideration of chemical and physiological disturbances and on the correction of them by administration of fluids The following determinations are made (1) The sodium and chloride levels of the blood must be known In some cases these levels are low requiring the administration of sodium and chloride in others they are elevated calling for

restriction of sodium and chloride (2) The carbon dioxide combining power of the blood must be known Usually an acidosis is present but sometimes alkalosis is found and appropriate treatment must be given (3) The albumin globulin ratio of the blood must be determined When hypoproteinemia is present it is corrected by giving protein intravenously or orally Knowledge obtained from these *determinations* is indispensable in the successful treatment of uremia In most cases the proper use of 5 and 10 per cent glucose solution sodium chloride solution plasma and solutions of albumin *sodium bicarbonate* and lactate will *accomplish* all that is possible Diminution in the output of urine which leads to retention of nitrogenous substances in the tissues and blood is the commonest defect and it may be corrected by *intravenous administration* of 1000 cc of 5 or 10 per cent glucose solution This may be repeated two or three times a day depending upon individual requirements

Sometimes it is wise to give *1000 cc* of five per cent glucose in isotonic saline because there is a loss of sodium chloride in some patients with uremia especially if vomiting precedes coma In nephritis before uremia sets in there may be difficulty in excreting sodium chloride Then later when uremia develops there may be hypochloremia which if uncorrected by the judicious use of sodium chloride may in itself cause added kidney damage Therefore in some instances a solution containing both glucose and saline is administered and in others glucose alone

It is always desirable to determine precisely the sodium and chloride levels of the blood When in doubt solutions of five or ten per cent glucose are safe if given at the rate of 5 or 10 cc per minute In the presence of an impaired circulation the rapid intravenous administration of any fluid may lead to further damage As a general rule solutions of sodium chloride may be used safely when dehydration is present without a rising nonprotein nitrogen of the blood An excessive amount of sodium chloride intravenously may cause edema and diminish the output of urine

A common defect is hypoproteinemia which may be corrected by the use of 200 cc of plasma daily for several days Solutions of albumin are also effective Amigen may be given intravenously for hypoproteinemia Amigen contains all the essential amino acids and 1 gram is equivalent to 1 gram of protein For intravenous ad

ministration amigen is dispensed in liter flasks containing 5 per cent amigen in 5 per cent glucose solution This liter contains 50 grams of protein 50 grams of glucose 2 grams of sodium chloride Two liters a day provide a normal adult with proper protein and salt requirements Amigen and other substances of like nature also are dispensed in powder form One tablespoonful 8 times a day is recommended in some cases

When a patient develops oliguria or anuria and uremia it is assumed that not only azotemia but also acidosis is present Sixth molar sodium lactate solution is used to combat acidosis This preparation is a stable isotonic solution of sodium r lactate in distilled water prepared for intravenous injection On injection of sodium lactate one half is converted into liver glycogen the other half is oxidized to bicarbonate directly One thousand cc of ⅙ molar lactate is equivalent to 340 cc of 5 per cent sodium bicarbonate solution in neutralizing acidosis In severe acidosis 40 to 50 cc per kg of body weight or *2000 to 3000 cc may be given daily*

While maintenance of proper fluid balance is vitally important within recent years fluids have been administered promiscuously Too much fluid is particularly dangerous to older patients and to patients with impaired cardiac reserve such as occurs in chronic nephritis No tests of cardiovascular integrity enable *the clinician* to determine beforehand if the cardiovascular system will tolerate fluid therapy One must follow the clinical rule that in the presence of definite clinically demonstrable heart disease with a history of symptoms past or present fluids are used intravenously only if indications are present and then in as limited amounts as *possible* administered slowly Isotonic solutions in volumes up to 3000 cc daily in 1000 cc doses at rates of injection from 20 to 50 cc per minute may be given without demonstrable cardiovascular changes in non cardiac patients and cardiacs in Grades I or II compensation In cardiac patients of Grades III or IV compensation isotonic *solutions* in 1000 cc volumes are definitely dangerous at rates of injection between 20 to 50 cc per minute

2 The use of diuretics There is a natural tendency for the physician in charge of a patient with anuria and uremia to wish to give something to stimulate the kidneys to further action The various diuretics naturally come to mind but those commonly used to

make the urine flow in cases of heart failure as the mercurials and diuretin are of very little value and may cause actual harm in uremia Probably the most important diuretic of service in cases of uremia is aminophylline given in 0 53 Gm (8 gr) doses intravenously along with 50 cc of 50 per cent glucose The aminophylline has a tendency to increase the capillary activity and thereby may be helpful

3 When the kidneys are functioning insufficiently it is traditional to attempt to relieve the body of the by products of metabolism through extrarenal routes Sweating for example the hot pack is one of the oldest measures in treatment While it is recognized that the hot pack does not eliminate very much of the waste by the sweating process itself it has another action which may be of some importance It may act as a counterirritant and in that way promote renal activity The hot pack is justified not because of any scientific reason but merely because it appears to do good in certain cases

4 The diet in uremia assumes rather a small place in treatment because the patient s gastrointestinal tract is usually unable to retain food After the episode of intoxication passes over diet assumes some importance it should be high in carbohydrate low in protein and rich in the various essential vitamins This is easily fulfilled by giving the patient cereals ice cream fruit juices gelatin and similar types of nourishment When vomiting nausea and abdominal distention become distressful one s therapeutic ability is usually strained to the utmost Frequently however the following preparation may be of some aid tincture of belladonna 16 Gm (4 drams) and elixir of phenobarbital 120 Gm (4 oz) one teaspoonful three times daily If this cannot be taken by mouth 15 Gm (½ oz) may be given per rectum and repeated every hour or two Sometimes it is necessary to give atropine 0 0004 Gm (1/150 grain) hypodermically

5 The cerebral manifestations such as sleeplessness delirium or coma may be the most prominent features of an early uremia The treatment of these manifestations requires considerable judgment A hot bath or warm pack may be satisfactory in relieving the restlessness and delirium Bromides given alone or in combination with chloral in doses of 1 33 Gm (20 grains) each are of outstanding

ministration, amigen is dispensed in liter flasks containing 5 per cent amigen in 5 per cent glucose solution This liter contains 50 grams of protein 50 grams of glucose 2 grams of sodium chloride Two liters a day provide a normal adult with proper protein and salt requirements Amigen and other substances of like nature also are dispensed in powder form One tablespoonful 8 times a day is recommended in some cases

When a patient develops oliguria or anuria and uremia it is assumed that not only azotemia but also acidosis is present Sixth molar sodium lactate solution is used to combat acidosis This preparation is a stable isotonic solution of sodium r lactate in distilled water prepared for intravenous injection On injection of sodium lactate one half is converted into liver glycogen the other half is oxidized to bicarbonate directly One thousand cc of ⅙ molar lactate is equivalent to 340 cc of 5 per cent sodium bicarbonate solution in neutralizing acidosis In severe acidosis 40 to 50 cc per kg of body weight or 2000 to 3000 cc may be given daily

While maintenance of proper fluid balance is vitally important within recent years fluids have been administered promiscuously Too much fluid is particularly dangerous to older patients and to patients with impaired cardiac reserve such as occurs in chronic nephritis No tests of cardiovascular integrity enable the clinician to determine beforehand if the cardiovascular system will tolerate fluid therapy One must follow the clinical rule that in the presence of definite clinically demonstrable heart disease with a history of symptoms past or present fluids are used intravenously only if indications are present and then in as limited amounts as possible administered slowly Isotonic solutions in volumes up to 3000 cc daily in 1000 cc doses at rates of injection from 20 to 50 cc per minute may be given without demonstrable cardiovascular changes in non cardiac patients and cardiacs in Grades I or II compensation In cardiac patients of Grades III or IV compensation isotonic solutions in 1000 cc volumes are definitely dangerous at rates of injection between 20 to 50 cc per minute

2 The use of diuretics There is a natural tendency for the physician in charge of a patient with anuria and uremia to wish to give something to stimulate the kidneys to further action The various diuretics naturally come to mind but those commonly used to

attached sodium accumulates in the blood stream Owing to a reduced blood volume the circulation slows down the blood pressure may fall and the concentration of the serum involves increase of the colloid osmotic pressure of the blood The decrease of blood pressure and the increase of osmotic pressure together result in reduction of filtration pressure This in addition to diminution of blood flow is the chief factor in reducing glomerular filtration

Diagnosis From a diagnostic standpoint there are three important features (1) Excessive vomiting or diarrhea from a gastro intestinal disorder often pyloric obstruction from an old peptic ulcer (2) the blood chlorides drop from a normal of 350 mg % to as low as 200 mg % This loss of chlorides is associated with an increase of the carbon-dioxide combining power of the blood which rises to as high as 90 to 100 volumes per cent in some cases (3) an azotemia with an increase of the nonprotein nitrogen to high levels A diagnosis of uremia may be made and the hypochloremic complications over looked unless a complete study of the electrolytes of the blood is made

Prognosis The outlook in extrarenal uremia depends upon the nature of the causative disease Frequently when the electrolyte bal ance is restored hydration corrected and the circulation improved the results of treatment are very gratifying

TREATMENT

The treatment of extrarenal uremia involves replacement of water sodium and chloride maintenance of normal circulation and blood volume and removal of the cause of the episode Shock if present must be combated and blood transfusions probably will be valuable

1 Restoration of extracellular electrolytes and water is accom plished by subcutaneous or intravenous infusions of sodium chloride or one of its modifications An intake of from 3000 to 5000 cc of fluid may be required

2 For the alkalosis administration of ammonium chloride by mouth or parenterally is recommended Sometimes intravenous in fusion of normal sodium chloride solution or hypertonic sodium chloride solution corrects the defect

3 If hypoproteinemia exists intravenous amino acids or blood plasma or both are given

help If the patient is unable to swallow these preparations they may be given by rectum If these simple remedies fail one is justified in administering hypodermically pantopon 0 02 Gm (⅓ grain) dilaudid 0 003 Gm (¹⁄₂₀ grain), or morphine 0 015 Gm (¼ grain)

6 Peritoneal irrigation in the treatment of uremia has been discussed at length by many and while it obviously has many possibilities its proper application demands the highest technical nursing and chemical care

EXTRARENAL UREMIA

Genuine uremia is a complication of nephritis obstruction to the urinary tract and degenerative and inflammatory diseases of the kidney In the absence of these diseases it is less commonly found but it may occur Extrarenal uremia is a clinical condition characterized by elevation of blood nitrogen dehydration due to loss of extracellular fluid and electrolytes normal or low blood pressure and oliguria which may progress to anuria

Etiology and Pathology Extrarenal uremia is the result not of organic disease of the kidney itself but of disturbances in metabolism hydration and of the electrolyte pattern of the body produced by a variety of diseases Although the kidney does not appear to be damaged undoubtedly in extrarenal uremia there is a functional disability unassociated with the classic diseases of the kidney Almost any serious illness or severe injury may be a precipitating cause Intestinal obstruction excessive vomiting or diarrhea from any cause gastrocolic fistulas and any condition which causes dehydration and elimination of chlorides from the gastrointestinal tract

Signs and Symptoms On physical examination the patient is usually irrational and appears to be in a state common to that of shock Examination reveals sunken eyes dry skin a dry and chapped mucous membrane and a frequent but small pulse Edema is never present Sometimes the blood pressure may be low but it is never elevated There is usually either oliguria or complete anuria and signs of dehydration are present due to a loss of fluid volume chiefly in the extracellular compartment Along with this dehydration there is a loss of extracellular electrolytes which leads to hypochloremia Frequently the hypochloremia is followed by alkalosis due to the fact that chlorides are not absorbed and an excessive quantity of un

principally in necrosis of the epithelium of the distal convoluted tubules In both conditions the underlying mechanism is vasoconstrictive renal ischemia resulting in oliguria the vasoconstriction resulting from a vasoconstrictor present in blood liberated from injured tissues Formation of this condition seems to be due in part to circulatory failure and consequently it should be slowed by restoration of circulation

A type of anuria occurring in cases of crush syndrome has recently been described by Trueta and associates A diminution in caliber of the renal artery and a diversion of the intrarenal blood flow from cortex to medulla was demonstrated by them in dogs submitted to a form of trauma designed to simulate crush injury Changes in renal circulation were thought due to neurovascular reflexes initiated in the injured limb since similar changes were produced by stimulation of various nerves These experiments lend support to the theory that renal anoxia plays an important part in the development of renal failure in crush syndrome

Signs and Symptoms Crush injury may be suspected in any case with a history of a crushed limb or occlusion of arterial supply for several hours After being released from the debris the patient s limb usually swells becomes hard and paralysis may exist Gangrene may occur If damage to the necrotic muscle is such that it causes great plasma loss [illegible] on may result followed by a blood pres

[illegible] no longer compensates for continued

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[illegible] irregularities may occur

[illegible] s typical of potassium

[illegible]

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[illegible] otassium retention

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4 The treatment is never complete until the pyloric obstruction or gastrointestinal defect which caused the condition is corrected

CRUSH INJURY

Crush injury is an entity reported by Minami as occurring in soldiers during World War I but which attracted little attention until Bywaters and Beall rediscovered it renamed it and reported four cases occurring during the air raids on London during 1940 It may be defined as a condition of shock followed by renal failure resulting from trauma

The syndrome is divided into two episodes (1) Traumatic shock which develops soon after release of compression and which if adequately treated may be controlled within 24 hours and (2) Symptoms of renal failure which develop the third or fourth day after injury

Etiology As yet the cause and pathogenesis of the lesion have not been established Some authors believe the condition is probably due to several factors in combination such as a degradation of products of myoglobin and hemoglobin products of tissue breakdown physiochemical alteration of blood and body fluids shock and disturbance of renal blood flow resulting in ischemia of the kidney and anuria

Further research on the etiological considerations of both myohemoglobin and hemoglobin compounds must be made to determine how they are excreted by the kidneys why they are precipitated in the lower segments and whether they are toxic

Pathology Changes observed in the kidneys are not distinctive Usually they are swollen their weight is increased and there is a white zone in the cortex The capsule strips easily to leave a smooth surface which may be mottled The cut surface is wet shiny and edematous and the cortex swollen and everted The capsular space is filled with granular eosinophilic debris and the capsular lining cells are changed so that the tubular epithelium appears to extend into the capsule to form a funnel like opening The tubules show degenerative changes in their epithelium and are full of pigmented casts The crushed muscle is pale with areas of hemorrhage and necrosis

Corcoran and Page have divided crush syndrome into two groups (1) Those in which the peripheral lesion is obstruction of the renal tubules by pigmented casts and (2) those in which the injury lies

long as pigment is excreted Mercurial diuretics are absolutely contra indicated

Prevention of the fall of renal blood flow is also of importance Restitution of lost plasma and extracellular fluid by transfusion of plasma and crystalloid solutions such as saline or lactate should be ordered

In treating shock plasma or serum is given if the blood pressure falls In severe cases or if hemorrhage has occurred whole blood may be necessary Morphine may also be given to relieve pain

The injured limb if ischemic should be kept cool with ice bags as this decreases the rate of autolysis and the living tissue is enabled to survive on a smaller blood supply Pressure bandages have produced satisfying results for some authors but others feel that their use in limiting plasma loss is potentially dangerous as in some cases the in crease in intramuscular pressure is in itself adequate to obliterate traversing blood vessels against the encircling fascial sheaths Tight binding would only increase this tendency

If circulatory obstruction occurs fascia splitting incisions may be made along the course of the main vessel once the urine is alkaline If obstruction is caused by spasm stripping or resection of the damaged part of the vessel may restore circulation Amputation should be a last resort and done only if the limb is so severely damaged as to be useless Decapsulation of the kidneys has been tried in cases of renal failure without much success

ACUTE SUPPRESSION OF URINE

Acute suppression of urine is a failure of secretion by the kidneys It must be differentiated from acute retention of urine in which urine is secreted by the kidneys and retained within the bladder

Etiology and Pathology Failure of the kidneys to secrete urine is brought about by (1) congestion associated with acute nephritis (2) mechanical obstruction of the urinary tract by stone in the ureters or renal pelves or by ureteral strictures neoplastic growths in the ureters or embolism of main vessels of both kidneys (3) bilateral necrosis of the cortex of the kidneys as seen occasionally in accidents of the puerperium and debilitating diseases (4) degen erative nephritis due to poisoning by or from the heavy metals (5) dehydration (6) retention of fluid in tissues (7) low blood pressure

will return to normal within approximately 6 months in patients with no sign of renal impairment the urine is less acid and a bright red

Diagnosis This condition may be strongly suspected in patients who after a crushing injury develop oliguria albuminuria hematuria and evidences of shock Examination of the urine blood and blood pressure and careful investigation of the intake chart will aid the diagnosis Hematuria from direct injury and hemoglobinuria from cold may be differentiated by examination of the urine and by use of a spectroscope If limb swelling is due to hematoma wheals are absent and the muscle is not doughy to the touch

Prognosis Prognosis is dependent upon the degree of shock and extent of the injury as well as the degree of hemoconcentration oliguria and blood rise Once severe renal insufficency has become apparent however death within a period of about 7 to 10 days is the ultimate outcome About one third of the patients with crush syndrome recover but these usually show a smaller volume of *necrotic* muscle damage than patients who die

TREATMENT

In the treatment of crush injury the following are basic preventive measures (1) Pressure bandaging of the injured limb (2) restoration of blood volume and blood pressure by controlling shock (3) adequate fluid intake and (4) the use of an alkali such as sodium bicarbonate or some other preparation for control of an acid urine

Although the natural tendency in therapy is to treat the shock first and then the local limb condition Bywaters believes the primary aim is to prevent development of renal failure This may be accomplished by administering alkaline substances as soon as possible Sodium bicarbonate or other mild alkali 4 Gm hourly by mouth will usually bring about alkaline diuresis within 12 hours If vomiting *prevents oral administration or if quicker alkalinization is required* 1 liter of isotonic sodium lactate given intravenously will produce the desired results *After a 12 hour period if diuresis cannot* be attained renal damage can be strongly suspected and further administration of alkali and fluid should be discontinued promptly Their use would prove dangerous since alkalosis develops readily in patients with renal failure If diuresis does occur alkalinization is continued as

2 Hot packs to the kidney area vigorous purging and hot colonic irrigations have demonstrated their value

3 A spinal tap is indicated at times when an increased intra spinal pressure is associated with the nitrogen retention

4 Surgery is imperative when the anuria is caused by local ob struction which cannot be removed by retrograde examination of the urinary tract If the suppression lasts more than a few days surgery to decapsulate the kidney must be tried even if there is no local obstruction

5 Adrenalin ½ to 1 cc (7½ to 15 minims) of a 1 1000 solution subcutaneously has been shown to release the suppression that is brought about by reflex action A nitroglycerin tablet 0 0006 Gm (1/100 grain) placed under the tongue may also be tried and at times has been effective in relieving the suppression

RENAL COLIC

Renal colic is an abdominal pain of extremely severe degree caused by the passage of a renal calculus down the ureter

Etiology and Pathology Renal stones are concretions formed from substances normally in solution in the urine A urinary stone or calculus is a body resembling a stone in its general characteristics and formed of crystalline urinary salts (exceptionally of other sub stances) held together by viscid organic matter and showing micro scopically or to the naked eye laminated structure (Keyes) Primary stones develop in an acid urine without antecedent inflammation while secondary stones form in alkaline urine which is the result of in fection The primary stones are composed usually of uric acid calcium oxylate and the urates of sodium calcium or potassium The sec ondary stones are formed of mixed phosphates of ammonium mag nesium or calcium There are various theories why solids ordinarily in solution in the urine are deposited as concretions Among the causes listed as responsible for stones are absence of non albuminous colloids the reaction of the urine stasis infection dietary deficiency and hyperparathyroidism

The renal calculus is formed in the pelvis and may remain in the kidney or pass down into the bladder The pain which is produced is felt to be due to excitement of violent spasmodic contractions along the ureter

simulating shock and (8) endocrine factors There are innumerable rare conditions which may be responsible for acute suppression of the urine Reflex anuria caused by the passing of a catheter has been known to occur rarely The hydronephrosis which so frequently accompanies partial obstruction of the urinary tract does not usually appear in acute suppression of urine

Signs and Symptoms There may be remarkably few symptoms Headache dyspnea vomiting and lumbar pain are most commonly seen Convulsions occur rarely and consciousness is not lost until shortly before death The severity of the symptoms of anuria varies directly with its duration which may be for hours or days A distinction from retention of urine may be made by examination of the abdomen or by catheterization

Obviously little if any urine is obtained What little is found may reveal evidence of acute nephritis or other manifestations of the cause of the anuria Retention of nitrogen occurs in the blood frequently in larger amounts than during the terminal stages of long standing nephritic uremia Pyelographic visualization of the urinary tract may reveal the cause and avenue of treatment of the condition

Prognosis The prognosis in acute suppression of urine must always be guarded It obviously depends on the cause of the disorder The earlier diuresis is resumed the better the outlook Recovery has been reported however after total suppression of urine for 19 days

TREATMENT

1 Suppression of urine caused by acute nephritis or by degeneration or necrosis of the kidneys requires that large quantities of fluid be offered to the kidneys to aid in opening their channels Isotonic fluid 3000 to 5000 cc of five per cent glucose in normal saline administered intravenously and subcutaneously should be given daily for its hydrating effect and hypertonic glucose 100 cc of a 20 per cent solution intravenously twice daily for its diuretic effect Sometimes it is advisable to withhold fluids entirely for a few days and then give a rather large quantity to obtain the desired response It is obvious that one must not continue giving intravenous fluids in large quantities when the output of urine is very low Such an error would lead in most cases to cardiac failure and pulmonary edema

taneously in an attempt to bring about ureteral relaxation Nitroglycerin 0 006 mg ($\frac{1}{100}$ grain) is beneficial at times

2 Local application of heat or a hot bath is comforting and upon occasions this procedure is sufficient to relieve the spasm

3 Relief of the anuria may be secured by the intravenous injection of 50 to 200 cc of 50 per cent glucose solution or the administration of 1000 to 2000 cc of five per cent glucose in physiological saline intravenously Colonic irrigations and purging may be tried in an effort to relieve the anuria

4 Glycerin in doses of 60 cc (2 ounces) three times daily for three days has been recommended as an aid in the passage of renal stones

5 Acidification of urine by administration of ammonium chloride 1 Gm (15 grains) four times daily and sodium acid phosphate 0 66 Gm (10 grains) four times daily is recommended

6 Hyperparathyroidism may have to be corrected by surgery

7 If the stones are phosphatic they may be dissolved by a solution consisting of citric acid (monohydrated) 32 25 Gm magnesium *oxide (anhydrous) 3 84 Gm sodium carbonate (anhydrous) 4 37* Gm and water to make 1000 cc A roentgenogram will help determine whether or not the stone is of a type which will respond to this treatment and an air pyelogram aids in showing its exact position The apparatus used depends on the case The pressure in the kidney should be sufficient to force the solution around the stone but the solution should not be forced around the stone continuously as this may cause a pyelonephritis If only one ureteral catheter is used a bladder catheter should also be employed to prevent the irritation which may occur as a result of voiding around the ureteral catheter A soft rubber catheter (Bardam No 10) may be left in place for weeks or months The apparatus may be so adjusted that the patient can operate it himself The progress of the dissolution may be checked by air pyelograms While this therapy is being used sulfonamide medication is advised to prevent or combat infection

PYELONEPHRITIS

Pyelonephritis is an infectious disease of the kidney pelvis and parenchyma

Signs and Symptoms The pain of renal colic is one of the most severe known and it may resist large doses of morphine It begins suddenly often in a person otherwise in the best of health and radiates across the abdomen, is referred to the region of the kidney and ultimately down the course of the ureter to the bladder symphysis pubis genitalia or the inner side of the thigh It is often accompanied by retraction of the testicle *the radiation* corresponding roughly to the progress of the stone down the ureter Faintness nausea vomiting cold sweat and shock accompany the pain Often there is incipient stimulus to urinate and urination becomes very painful The urine is scanty high colored and frequently bloody The manifestations are related to the size of the calculus Palpable enlargement of the kidney occurs in 10 to 25 per cent of cases and is presumably due to hydronephrosis or pyelonephrosis Ten to 20 per cent of cases are bilateral

Albuminuria hematuria and pyuria of varying degrees are present Calculi may be found in the strained urine Roentgen examination of the abdomen may reveal the presence of stones with or without pyelography

Complications include obstruction ulceration and infection Hydronephrosis may be a sequela The obstruction if complete may cause *anuria of the affected kidney Complete anuria* ensues when both kidneys are blocked simultaneously Ulceration is more likely to occur with a larger and less moveable stone and may cause perforation and extravasation of urine Ureteral stricture may result from an impacted stone Renal calculi are among the commonest causes of infection of the kidney particularly with staphylococcus albus

Prognosis When anuria persists more than a few hours the chance of spontaneous recovery is diminished but removal of the stone by manipulation or operation makes the prognosis better The conditions responsible for the formation of calculi continue after their removal and in many cases lead to new concretions

TREATMENT

1 The relief of pain usually requires morphine 0 016 to 0 032 Gm (¼ to ½ grain) repeated in the space of an hour to secure relief Atropine 0 006 Gm (1/100 grain) may be given simul

severe cases in milder cases only tenderness over the involved kidney is elicited by pressure The pain may extend anteriorly to the region of the gallbladder or even as low as the appendix radiating across the abdomen Hypertension may be a direct result or it may exist coincidentally In chronic cases the damage may be sufficient to cause symptoms of uremia

Diagnosis An accurate diagnosis of pyelonephritis is based on the history and physical examination urine examination and cystoscopy and ureteral catheterization The urine findings show leukocytosis and bacteria Albumin and white blood cells frequently clumped are always present in the urine unless there is a local obstruction to the urinary flow on the corresponding side as is occasionally found at the beginning of the disease Casts are more commonly absent Red blood cells are rarely abundant enough to cause manifest hematuria but they may be found under the microscope The urine is scanty and high-colored in the acute cases but may be increased in amount and of low specific gravity in the more chronic cases in which there is severe renal damage All grades of functional impairment of the kidney may be encountered as evidenced by lowering of the specific gravity of the urine increase in the volume of the night urine poor response to renal function tests and nitrogen retention in the blood There may be changes in the pyelographic picture and exact differentiation between various renal diseases may require ureteral catheterization and pyelography

Prognosis The prognosis of pyelonephritis depends upon a variety of factors including the virulence of the organism the location of the lesion in regard to drainage and the degree of renal damage Infections by the pyogenic cocci are more dangerous than those caused by the colon group The more the lesion is confined to the pelvis and the less it involves the parenchyma the better will be the chance of resolution Obstructions must be removed from the urinary tract as soon as possible for a satisfactory outcome to be anticipated The course of chronic pyelonephritis depends on the extent of the lesion Repeated infection may lead to septicemia or uremia

TREATMENT

Essentially the treatment of pyelonephritis includes relief of any obstruction present bed rest diuresis with water urinary antiseptics and occasionally drainage

Etiology Pyelonephritis is caused most commonly by the Bacillus coli pyogenic cocci and at times by the tubercle bacillus The Bacillus coli and related organisms are present in two thirds of the cases and have a tendency to involve the pelvis of the kidney more than the parenchyma The pyogenic cocci include the Staphylococcus aureus and albus, the streptococcus and pneumococcus and rarely the gonococcus At times other infecting agents as the Bacillus proteus the Bacillus pyocyaneus the Bacillus influenzae and the Actinomyces bovis are isolated The pyogenic cocci tend to affect the parenchyma of the kidney and cause perinephritic abscesses Bacteria are transported to the kidney by the blood or by extension up the ureter The latter may be due to reflux of urine with inflammation of the ureter or to obstruction of the lower urinary tract Other routes of infection are the lymphatic system and more rarely by direct extension from neighboring organs Bacteria may pass through the kidney without causing any apparent harm a notable example of which is the typhoid bacillus Lowered resistance of the kidney to infection is probably brought about by stasis as a result of conditions such as hydronephrosis and calculi Ascending infection by the colon bacillus is found relatively frequently in young girls pregnant women and elderly men

Pathology In addition to the inflammatory reaction found in the mucous membrane of the renal pelvis and lower urinary tract lesions consisting of round cell infiltrations are found early about the tubules These round cell infiltrations may break down into abscesses The end result is the formation of scar tissue and consequently the tubules are distorted or destroyed In the chronic form of the disease the pathology resembles grossly that of chronic glomerulonephritis with adherent capsule loss of normal markings and a thinned parenchyma The calyces become dilated old scars are found in the renal tissue and the walls of the renal pelvis are hypertrophied and thickened

Signs and Symptoms The onset is frequently sudden with chills fever pain and tenderness in the involved kidney area frequent and painful urination and the presence of bacteria pus and albumin in the urine The fever varies from a brief rise to a fulminating septic curve A distinct chill occurs in the more severe cases Pain in the costovertebral angle is caused by stretching of the kidney capsule in

mandelic acid 3 Gm (45 grains) with ammonium chloride 1 Gm (15 grains) administered four times a day and the ketogenic diet In giving mandelic acid the urine must be kept highly acid the pH not rising above 5 3 Excessive acidification of the urine however is undesirable in cases of renal insufficiency acidosis or the very acute stages of pyelonephritis

6 Streptomycin 2 Gm (2 000 000 units) daily divided into 8 doses for about one week may prove effective if other measures of therapy fail

7 Most subacute or chronic renal infections are caused by stasis and the obstruction must be removed before further treatment will be efficacious

Renal Damage Due to Sulfonamides

The kidneys may be damaged in the course of sulfonamide therapy This toxic reaction its treatment and prevention will be taken up in Chapter XXIV

1 Bed rest is essential in the acute stages with fever and is recommended for all cases where there is extensive involvement of the kidney

2 The diet should be nourishing and contain a moderate amount of protein Three thousand to 5000 cc of fluid a day are required The kind of fluid to be used depends on whether or not acidosis is pending Ten per cent glucose in normal saline is useful but ⅙ M sodium lactate is needed if the alkali reserve is lowered

3 *Heat applied to the kidney area aids in the relief of pain* If further relief is required mild measures, as a combination of codeine sulfate 0 016 Gm (¼ grain) phenobarbital 0 06 Gm (1 grain) and acetylsalicylic acid 0 33 Gm (5 grains), should be tried before resorting to heavier opiates

4 The favored urinary antiseptics at present are the sulfonamide drugs sulfadiazine has been notably successful The drug need not be given in as high a dosage as for pneumonia and similar septic states it is not necessary that a high blood level be maintained for adequate concentration of the drug is obtained in the urine with low blood levels Dosages of 0 5 Gm to 1 0 Gm (7½ to 15 grains) three to four times a day have proved sufficient Precipitation of sulfonamide crystals is thought to be less frequent when coincidental alkaline therapy as sodium bicarbonate 0 66 Gm (10 grains) with each dose is employed The urine should be watched carefully for the presence of drug crystals and for evidence of further renal irritation by the drug It has been shown that where there is a tendency to recurrent urinary tract infection as in cases of irreparable deformities of the urinary tract or where the necessity of frequent catheterization exists very small doses of sulfadiazine as low as 0 13 Gm (2 grains) five times a day prove an excellent prophylactic remedy When the kidney infection is caused by the nonhemolytic streptococcus or staphylococcus penicillin 100 000 units intramuscularly every three hours will usually bring about gratifying results

5 Urinary antiseptics such as hexamethylenamine and sodium acid phosphate may be given in doses of 12 to 15 Gm (40 to 50 grains) three times a day Other methods of urinary antisepsis that have been used with notable success are urotropin *0 33 Gm* (5 grains) and sodium acid phosphate 0 33 Gm (5 grains) with ammonium chloride 0 66 Gm (10 grains) administered three times a day or

3 *Primary atypical pneumonia of unknown etiology*
4 Bwamba fever
5 Encephalitis and encephalomyelitis
6 And others

B Between Virus and Rickettsia
1 Psittacosis—specific
2 Ornithotic pneumonias
3 Epidemic keratoconjunctivitis
4 Lymphogranuloma venerum

C Rickettsia *(vector—tick except Australian Q fever)*
1 Typhus
a Epidemic
b Endemic
c Trench fever
2 Tsutsugamushi fever group
a Scrub typhus
b Malayan typhus
c Sumatran mite fever
d *Oroya fever of Peru*
3 Spotted fever group
a Rocky Mountain spotted fever
b Fievre boutonneuse
c Sao Paulo typhus of South America
d South African tick fever
e Montana fever (Nine Mile Creek fever)
f Australian Q fever
g *American Q fever*

III Other agents (Usually bronchopneumonic)
A Chemicals—liquids gases etc
B Foods—*aspiration pneumonitis* etc
C Allergy— Loeffler s transitory pulmonary infiltrations

Lobar Pneumonia

Lobar pneumonia is an acute medical emergency and the advent of the newer specific therapeutic measures requires that the diagnosis be made as soon as possible so treatment may be commenced early in the disease While the specific remedies as serum and chemotherapeutic measures are sometimes effective when given late in the disease they are much more beneficial when administered in the earlier periods of the infection Lobar pneumonia is a specific acute infectious disease which involves an entire lung or part of a lung sometimes both lungs are completely involved in the pneumonic process In contradistinction to bronchopneumonia lobar pneumonia is al

CHAPTER XIII

The Lungs

PNEUMONIA

Pneumonia is an acute inflammation of the lungs usually caused by the pneumococcus It may be of the lobar bronchial interstitial or combined forms but lobar and bronchopneumonia are the commonest types The pneumococcus causes most cases of lobar pneumonia and more than one half of the cases of bronchopneumonia The pneumococci in the blood stream are capable of producing diseases other than those of the lung However the chief manifestations are respiratory Other organisms as Streptococcus hemolyticus Friedlander bacillus Staphylococcus aureus or nonbacterial agents may cause pneumonia The importance of determining the causative agent cannot be overemphasized since effective treatment is dependent on it Pericarditis endocarditis or meningitis may be the sequelae of a general pneumococcal septicemia So called atypical pneumonia or virus pneumonia is not caused by the pneumococcus but probably by one of the numerous viruses This form will be discussed separately

The following table summarizes a modern classification of the acute pneumonias

THE ACUTE PNEUMONIAS

I Bacterial (organisms—pneumonia Staphylococcus Streptococcus Friedlander etc)
- A Lobar pneumonia
  - 1 Complete lobe
  - 2 Bronchopulmonary segmental type
- B Bronchopneumonia
  - 1 Nonsuppurative lobular type
  - 2 Suppurative type
  - 3 Gangrenous type

II Nonbacterial—Interstitial pneumonia (acute) The types are bronchitic peribronchitic and alveolar (singly or in combination)
- A Virus
  - 1 Influenza A and B
  - 2 Measles

3 Primary atypical pneumonia of unknown etiology
4 Bwambi fever
5 Encephalitis and encephalomyelitis
6 And others
B Between Virus and Rickettsia
1 Psittacosis—specific
2 Ornithotic pneumonias
3 Epidemic keratoconjunctivitis
4 Lymphogranuloma venerum
C Rickettsia (vector—tick except Australian Q fever)
1 Typhus
a *Epidemic*
b Endemic
c Trench fever
2 Tsutsugamushi fever group
a Scrub typhus
b Malayan typhus
c Sumatran mite fever
d Oroya fever of Peru
3 Spotted fever group
a Rocky Mountain spotted fever
b Fievre boutonneuse
c Sao Paulo typhus of South America
d South African tick fever
e Montana fever (Nine Mile Creek fever)
f Australian Q fever
g American Q fever
III Other agents (Usually bronchopneumonic)
A Chemicals—liquids gases etc
B Foods—aspiration pneumonitis etc
C Allergy— Loeffler s transitory pulmonary infiltrations

Lobar Pneumonia

Lobar pneumonia is an acute medical emergency and the advent of the newer specific therapeutic measures requires that the diagnosis be made as soon as possible so treatment may be commenced early in the disease While the specific remedies as serum and chemotherapeutic measures are sometimes effective when given late in the disease they are much more beneficial when administered in the earlier periods of the infection Lobar pneumonia is a specific acute infectious disease which involves an entire lung or part of a lung sometimes both lungs are completely involved in the pneumonic process In contradistinction to bronchopneumonia lobar pneumonia is al

ways a primary disease Bronchopneumonia frequently follows an upper respiratory infection or is a complication of some other disease in the body

Etiology Lobar pneumonia may occur at any time of the year but it is most frequent in the months from January until May It is

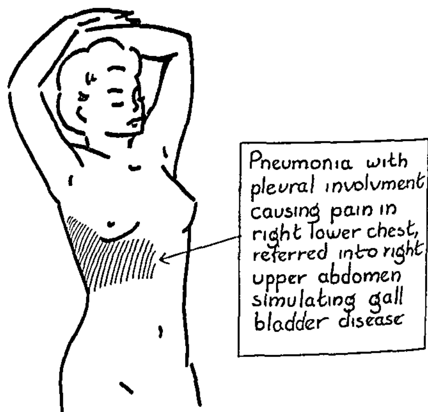


Fig 1—Pneumonia

a disease that spares no age group Exposure to inclement weather draughts loss of sleep and contact with patients who have infections or healthy carriers are the chief predisposing factors The specific cause of pneumococcic pneumonia of course is the *pneumococcus* Formerly four main types of pneumococci were recognized but recently more than 40 kinds have been identified Types I II III V VII VIII and XIV are responsible for the majority of cases of pneumonia Sometimes more than one type may be present in the same patient Types I II and V which are found most often in lobar pneumonia

usually present a fairly typical picture These types along with Types VII and VIII cause about 50 per cent of all cases of lobar pneumonia

Pathology Pathologically in response to the irritation produced by the pneumococci there is an outpouring of inflammatory exudate into the alveoli causing the air to become displaced and the lung at times to be converted into an airless organ

It has been customary to recognize four stages of pneumonia and in the clinical diagnosis it is very important to have these various phases of the disease in mind

1 Engorgement of the lung
2 Red hepatization
3 Gray hepatization
4 Resolution

Signs and Symptoms Pneumonia does not always follow the classical textbook description with chills fever pain in the chest and expectoration of bloody or rusty sputum It is well to remember that pneumonia is a disease that sets in abruptly and there may or may not be a preceding upper respiratory infection with a cough Frequently the first evidence of pneumonia is a feeling of prostration which is due to the early bacteremia followed by coughing and bloody expec toration Even at this early stage the sputum may contain the pneu mococcus When the patient has a chill with a rapid bounding pulse fever and pain in the side of the chest the diagnosis is easily made

Although pneumonia may be suspected when pleuritic pain chill fever tachycardia and bloody sputum occur the physical signs of pneumonia may not be present for another 24 hours The early recognition of pneumonia is accomplished by careful attention to the history of onset and by a skillful examination of the chest Many physicians believe that an x ray examination is more important in early diagnosis than a physical examination and that it is a more positive means of diagnosing early pneumonia This is not always true since proficient clinicians are able to determine the presence of pneumonia and clinch the diagnosis before the evidence is con firmed on the x ray film

Inspection usually reveals a patient with an anxious facial expres sion Breathing may be rapid and the excursions of the chest may be limited A cyanotic tinge about the lips or fingertips may help in the identification of the disease Palpation reveals a hot dry skin

and the pulse is not only rapid but bounding There may be no alteration of tactile fremitus The early diagnosis of pneumonia is established usually by the finding of an impaired percussion note over the diseased lung The dullness to percussion is usually well marked even in the first stage of the disease

Auscultation of the involved side of the chest may disclose alteration of the breath sounds Typical bronchial breathing may not be

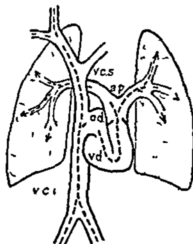


Fig 2—Infarction of the lung through sudden occlusion of a pulmonary artery by a blood clot (embolus) The embolus having become detached at some point in the inferior vena cava (v c i) or its tributaries or in the superior vena cava (v c s) or its tributaries passes through the right auricle (o d) is discharged into *the pulmonary artery (a p) and lodges in one of the lobes of the lung* giving rise to an infarct which finds its clinical expression in 1 a sudden sharp pain in the side 2 blood spitting (hemoptysis) 3 the physical signs shown in Fig 3 Usual causes in the order of their frequency 1 Infectious phlebitis particularly puerperal 2 heart disorders in the stage of lost compensation especially mitral disease in the *stage of dilatation of the right heart 3 after operations especially* abdominal and chiefly appendiceal and pelvic

present but a muffled tubular breathing is usually noted The presence of fine crepitant rales, especially if the patient coughs, associated with other signs is practically always positive evidence of early pneumonia Two or three days may elapse before the typical features of lobar consolidation appear

Diagnosis In those cases in which the area of pneumococcic consolidation begins deep in the lung and findings are not evident for several days the percussion note changes and distant or muffled bronchial breathing serve to identify the condition Sometimes the consoli

dation involves the lower lobe and the diaphragmatic pleura becomes inflamed In this case movement of the involved side of the chest is very limited and pain may be referred into the abdomen suggesting an acute abdominal disease Sometimes the pain may extend as low in the abdomen as the area of the appendix simulating acute appendicitis This is commoner in children than in adults

Pulmonary infarct as a result of an embolus may simulate pneumonia at times Bloody sputum chest pain fever and signs of consolidation may be very similar to the consolidation of pneumonia

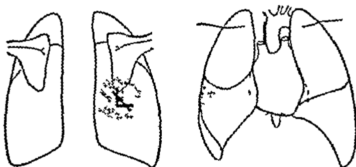


Fig 3—Physical signs of infarction of the lung through sudden occlusion of a pulmonary artery by a blood clot (embolus)

When there is doubt the treatment for pneumonia should be instituted at once The presence of pneumococci in the sputum or in the blood stream serves to make the differentiation positive In older individuals lobar pneumonia may be confused with coronary thrombosis Careful attention however to the onset may help in diagnosis Coronary thrombosis is apt to be associated with more evidence of collapse in the beginning than lobar pneumonia In lobar pneumonia the blood pressure is less likely to change In brief in coronary disease the cardiovascular features predominate while in lobar pneumonia the cardiovascular system is intact especially in the beginning of the disease It is only later that cardiovascular collapse is a feature

Usually the mistakes in diagnosis of pneumonia consist in failure to recognize the presence of the disease in its earlier stages Diagnoses such as bronchitis influenza pleurisy or grippe are occasionally made

instead of pneumonia Pulmonary tuberculosis typhoid fever or pulmonary embolism may simulate pneumonia so closely that a few days may elapse before the true diagnosis is made Since the early diagnosis of pneumonia is so important in the modern treatment of the disease it is better to treat the suspected case as one of pneumonia and learn later that it is another disease than to fail to recognize the presence of pneumonia in its early stages

If lobar pneumonia remains uncomplicated the disease runs its course in from 4 to 12 days terminating by crisis when the temperature drops and the pulse and respiratory rates suddenly approach normal At other times the resolution takes place more slowly and recovery is by lysis

A variety of complications may occur with lobar pneumonia Empyema is the commonest and usually develops after the seventh day of the disease However it may occur after the primary lobar pneumonia has practically subsided Whenever a patient with pneumonia appears to be making a satisfactory recovery and then suddenly has a relapse with a higher fever more rapid pulse rate and an increase of the respiratory rate one should always look for empyema Perspiration elevated white blood count and increase in polymorphonuclear leukocytes may be associated with the above signs Evidence of fluid is usually noted if the effusion is free in the pleural cavity and diminution or absence of tactile fremitus along with the other signs confirms the diagnosis If there is a question concerning a definite diagnosis chest plates and thoracocentesis are valuable aids

Failure of the pneumonia to resolve at the end of the tenth or twelfth day often leads to a diagnosis of unresolved pneumonia The supposed unresolved pneumonia however usually turns out in these cases to be empyema or abscess of the lung Otitis media and mastoiditis are complications of pneumonia and are usually found in children Other complications of pneumonia are pericarditis endocarditis and meningitis and any one of these deserves a very guarded prognosis

Bronchopneumonia

While lobar pneumonia is a term applied to consolidation of an entire lobe a lung or both lungs bronchopneumonia is a term

applied to areas of consolidation disseminated throughout both lungs The isolated small patches of consolidation may at times become confluent and make the diagnosis difficult

Etiology and Pathology Bronchopneumonia usually occurs in children under 12 years of age and in older people past 65 years As a rule it is secondary to other diseases such as acute bronchitis measles scarlet fever or it may be a complication of heart disease malignant disease or Bright s disease While lobar pneumonia is almost always produced by the pneumococcus other organisms as the streptococcus may be the cause of bronchopneumonia

The characteristic pathologic features are congestion of the bronchi often including the trachea Collapsed areas on the outside of the lung are frequently seen which are caused by the bronchioles becoming filled with secretion preventing air from entering the lobule This air when absorbed causes the lobule to collapse The parenchyma most frequently shows patchy consolidations and inflamed bronchi leading into the involved portions A thin purulent exudate may at times be found on the surface of the lung

Signs and Symptoms Bronchopneumonia does not set in abruptly as does lobar pneumonia It usually comes on gradually in an individual who is ill with some other condition The disease ends in lysis not by crisis as is usually the case in lobar pneumonia Cough pain in the chest shortness of breath and cyanosis usually mark the beginning of a bronchopneumonic process The physical signs are not nearly so characteristic as in lobar pneumonia and areas of consolidation may be completely obscured by an associated bronchitis or heart failure

Diagnosis Usually the breath sounds are decidedly altered on both sides of the chest below the angle of the scapula and the bronchopneumonic breath sounds associated with medium or small sized mucous rales usually lead to the diagnosis A characteristic feature of bronchopneumonia is the rapid change of signs from day to day The course of bronchopneumonia is usually longer than that of lobar pneumonia running from four to five days to two or three weeks It must also be remembered that in contrast to lobar pneumonia bronchopneumonia is caused by one of the higher pneumococci frequently in combination with other organisms and that the disease is most commonly observed in infants and in the aged In this disease

the differential diagnosis assumes great importance for tuberculous bronchopneumonia may simulate the nontuberculous kind very closely unless sputum is examined frequently for the presence of the tubercle bacilli

Prognosis The modern treatment of pneumonia has altered the prognosis so much within recent years that our ideas of a few years ago seem like century old ones Formerly from 25 to 40 per cent of patients with pneumonia died Now from three to nine per cent die In general it is difficult to give any prognostic rules The following suggestions as to prognosis may be helpful

1 If the patient with pneumonia shows serious evidences of intoxication by the fourth or fifth day of the disease the outlook is bad Such toxic manifestations consist of the relative condition of the heart the state of the blood pressure the rate of the pulse and the general condition of the patient

2 If the patient s heart blood pressure and pulse rate tolerate the infection well until the seventh day the chances for recovery are good

3 If the pulse rate per minute rises above the figure for the systolic blood pressure and continues to rise the prognosis is bad

4 A chronic alcoholic bears up poorly

5 Prognosis is serious in very young children and in adults over 40 years of age

6 Bacteremia leukopenia pregnancy and septic complications affect the prognosis unfavorably

7 The type of pneumococcus concerned influences the outcome Pneumonia due to pneumococcus Type I is more benign and that due to Types II V and VII usually more severe The seriousness of Type III pneumococcus pneumonia is variable

8 Some believe it is helpful in treatment and prognosis to determine the number of pneumococci in Wright stained smears of rusty sputum When the sputum count is 10 or less pneumococci per field the patient is only mildly ill If the count is between 11 and 35 per field the patient is moderately ill and if the count rises over 35 he is seriously ill

TREATMENT OF PNEUMONIAS

With the introduction of penicillin and chemotherapeutic measures the older and more general measures have been somewhat

neglected The treatment of pneumonia may be divided into two phases (1) The General Measures and (2) the Specific Therapeutic Agents

1 General measures

a Formerly it was thought that a patient with pneumonia should not be moved from his bed at home to a hospital because the moving was considered to be deleterious to the patient With the advent of penicillin and better hospital facilities it became more commonplace to take the patient to the hospital The administration of penicillin oxygen intravenous solutions and special nursing care could be furnished so much better that the old fear of moving the patient was almost completely cast aside At the present time it is difficult to say what the physicians of the future will do but it is probable that if a patient is in a comfortable home the treatment can be carried out just as well there as in the hospital Furthermore the cost of the treatment for the patient is so much less in the home that there may be a return to the use of specific measures there

b The patient should be kept comfortable and placed in a semireclining position if this is most pleasant Since pneumonia is a communicable disease the patient should be kept in a room by himself

c The patient should take at least 1500 to 2000 cc of fluid a day Intravenous injections of large amounts of glucose solution should be discouraged because they are not well tolerated by pneumonia patients On the other hand if the patient is vomiting and cannot take fluid by mouth the administration of glucose in saline intravenously may be considered provided the solution is given at a slow rate of speed (10 cc or less per minute) It is also to be remembered that the chlorides are low in pneumonia

d A soft liquid diet is best for the patient in the early stages of the disease but the type of food should be left to the discretion of the patient rather than to the nurse or physician It is senseless for example to force milk on a pneumonia patient who had always detested milk when he was well It may be added that a patient who is accustomed to taking tea or coffee is not harmed by a little tea or coffee when he is sick Fruit juices charged water lemon and orangeades and other fruit ades are usually well borne

e The room should be kept at a temperature of about 15 6 to 21 1 C (60 to 70 F) Visitors should be excluded if possible and precautions taken to protect the people who must come in contact with the patient

f The mouth should be kept clean and moist by the use of a mouth antiseptic dissolved in water

g The bowels should be kept active but not particularly loose

h Since coughing is apt to be distressful a cough mixture containing 0 016 to 0 032 Gm (¼ to ½ grain) codeine in some pleasant vehicle as syrup

of wild cherry may be given three or four times a day Later on ammonium chloride 0 66 Gm (10 grains) three or four times a day may be added to the cough mixture to stimulate the secretion of the bronchial mucous membrane If the patient is not alert enough to cough up the increased bronchial secretion this addition should not be made If necessary chest pain may be relieved by codeine sulfate or morphine Heat may also be applied to the site of pain

i Headache may be controlled by administering a capsule containing 0 032 Gm (1/ grain) codeine sulfate and 0 33 Gm (5 grains) acetyl salicylic acid

j Nausea vomiting and abdominal distention often disturb the pneumonia patient These may be relieved by oxygen therapy Therapeutic stupes and pitressin 0 5 to 1 cc hypodermically three or four times a day may be valuable adjuncts

2 Specific measures of treatment Specific measures may be enumerated under the headings of

a Penicillin

b Chemotherapeutic agents

c Serum

d Oxygen

Penicillin When penicillin is used in the treatment of pneumonia the dosage of the drug and the route of administration must be considered It is usual at the present to employ 300 000 to 400 000 units of penicillin daily Penicillin may be given intravenously intramuscularly or orally The continuous intravenous drip method may be employed in serious cases for the first day or two then the continuous intramuscular drip for a day or two and finally intermittent injections every three hours Many prefer the intermittent intramuscular injections to the other methods but it must be emphasized that each procedure has its adherents and antagonists No strict rule can be laid down for the length of administration of penicillin Usually active penicillin therapy must be continued for 5 or 6 days after the fever has gone and the patient seems cured Some advise the continuation of penicillin by mouth 600 000 units daily for several days after the fever has disappeared

The Comparative Value of Penicillin and the Sulfonamides At the present time there have been some reports which point out the comparative value of penicillin and the sulfa drugs in the treatment of pneumonia Several factors must be taken into consideration for example the cost of penicillin and the necessity of giving penicillin

parenterally The sulfonamides may be given by mouth and they are comparatively cheap although they are toxic for many individuals Serious complications may at times follow administration of the sulfonamide preparations In summary the advantages and disadvantages of these two therapeutic measures may be given as follows

	Penicillin	Sulfonamides
1	Expensive and less active given orally	Cheap plentiful and best given orally
2	Non toxic and quite safe	Often toxic and occasionally very dangerous
3	Allergic sensitivity infrequent and usually innocent	Allergic sensitivity frequent and dangerous
4	Therapeutic action not affected by number of bacteria blood serum pus or tissue autolysates	Therapeutic action often materially affected by numbers of bacteria etc
5	Concentration levels of the blood easy to determine which acts as a therapeutic guide	Concentration levels in the blood easy to determine which makes administration precise
6	There may be a more abrupt fall in temperature and a more rapid subsidence of symptoms	

In addition penicillin is the drug of choice in the following types of pneumonia cases (1) Those with sulfonamide resistant pneumonias (2) patients sensitive to the sulfonamides (3) patients with renal cardiac or hepatic damage (4) patients seriously ill with pneumococcic pneumonia and/or its complications

Chemotherapy The value of sulfonamides in the treatment of pneumonia is so well established that it is unnecessary to elaborate on their advantages Both sulfadiazine and sulfamerazine may be employed with good results

The general impression of chemotherapy may be summarized as follows

1 Sulfadiazine and sulfamerazine are effective in the treatment of almost any type of pneumococcus pneumonia The sulfonamides are capable of reducing the mortality rate from 30 to 40 per cent to the low figure of from four to five per cent Undoubtedly these statistics for fatality rates will have to be changed from time to time because of variations that occur from year to year in the severity of the

pneumococcus infections It is only natural that unless the diagnosis of pneumonia is made with great caution a false and probably too favorable view of the therapeutic effects of the sulfonamides and antibiotics may develop

2 Administration The initial dose of either drug is 4 Gm (60 grains) immediately followed by 1 Gm (15 grains) every 4 hours until the temperature drops to normal which occurs usually within 24 to 36 hours After the fever has subsided the drug should be continued for 2 or 3 days after apparent recovery so the pneumonia may be held under control One gram of soda bicarbonate is administered with each 1 Gm dose of the sulfonamide to maintain alkalinization Fluid intake of 1500 to 2000 cc daily is necessary Alkalinization and an adequate fluid intake have done much to reduce the occurrence of toxic reactions in sulfonamide therapy If the drug is discontinued too soon a recrudescence may follow excretion of the drug through the kidneys If this happens reinstate drug therapy starting again with the initial dose When the treatment is discontinued it should be done abruptly to eliminate the possibility of the patient becoming drug fast

Higher doses of 6 Gm (90 grains) at first followed by 1 Gm (15 grains) every four hours are attended by slightly more rapid recovery fewer relapses and less likelihood of spread of the pneumonia to another lobe or of delayed resolution Toxic reactions seem no more numerous with the large than the small doses

Both sulfonamide and serum therapy may be gauged and controlled by a study of the sputum count Determination of the number of pneumococci in Wright stained smears of rusty sputum from time to time will also enable one to evaluate the effect of therapy and the course of the pneumonic process

It is best to determine the level of the sulfonamide preparation in the blood stream by the Marshall method so the concentration of the free sulfonamide may be learned It is advised to keep the concentration at the optimal level during the first four or five days of treatment This level varies with the preparation in use

At the present time fairly satisfactory preparations for intravenous use are obtainable for patients who are unable to tolerate the drugs by mouth or when it is inadvisable to give them orally When there is intractable vomiting or inadequate absorption of the drug

after oral dosage or when it is not advisable to waste precious hours in trying to raise the blood concentration of the drug *via* oral administration the intravenous route should be used However this method should be abandoned as soon as it is possible or safe to give the drug orally

Certain complications which may result from sulfonamide therapy must be kept in mind

1 Kidney damage may occur as a result of mechanical blockage of the tubules or ureters by sulfonamide crystals or from parenchymal changes due to the nephrotoxic action of these drugs Hematuria and other evidences of renal irritation have followed the administration of sulfadiazine and sulfamerazine and fatalities due to oliguria or anuria have occurred Almost all patients who have received large doses have had crystals of the acetylated form in the urine These are usually seen without associated hematuria pus cells or albumin These typical boat shaped or spear head shaped crystals in most cases appear during the administration of the drug and quickly pass away when the drug is discontinued If a patient has nephritis or any other renal disease causing renal insufficiency caution should be practiced in the administration of the drug because there may be a rapid accumulation of the drug in the tissues with a toxic reaction However sulfonamides may in some cases cure acute glomerulonephritis and the kidney lesions instead of being made worse may disappear

Renal complications as hematuria albuminuria and anuria from plugging of the renal tubules and ureters with the acetylated compounds occur and when any of these unfavorable reactions develop the drug must be discontinued an abundance of fluids given to increase the urinary output and in the case of anuria the ureters must be washed out with a catheter

A few safeguards will protect the patient against the renal complications of sulfonamide therapy The intake of fluid the hydration of the patient s tissues and the output of urine are probably the most important factors concerning the kidney impairment General opinion is that 1500 to 2000 cc of fluid per day must be given if adequate urinary output is to be assured During therapy careful observations of the quantity of the urine and its appearance on gross and microscopic examination should be made If sulfonamide crys

tals are present extra care must be taken in regard to dosage blood level, and urinary output but this in itself is not an indication that therapy must be stopped When the urine is alkalinized to a pH of 7 or higher there is very little crystalluria Renal disorders should be carefully evaluated before beginning therapy

2 Nausea vomiting anemia or skin reactions may occasionally occur Vomiting however is no reason for discontinuance of the drug The tablet may be crushed and given in milk or fruit juice and after several doses the patient may tolerate the tablets even if he could not do so previously

3 The sulfonamides may cause fever This fever may lead one to believe that the original disease is not yielding to the treatment and the drug therefore is given in even greater doses than before The point to be remembered is that when the underlying disease seems to have responded to treatment and the fever continues discontinuance of the drug for a day may be followed by a drop of the temperature to normal

4 The patient may become resistant to sulfonamides If a patient who is originally sensitive to sulfonamides later becomes resistant he may pass this same strain of sulfonamide resistant pneumonia to another person who may develop pneumonia which will not respond to sulfonamide therapy However if an individual does not respond to a particular sulfonamide a switch to another drug of this group may be followed by good results

5 These drugs are contraindicated when there is a history of serious toxic reactions from previous medication with the sulfonamide group renal or hepatic disease or persistent vomiting especially in patients where the pneumonia develops after a gastrointestinal operation However in some cases it may be best to give the drug if there is a chance of saving life (See Chapter on the Sulfonamide Drugs)

Serum Treatment The use of serum in the treatment of pneumonia has become less prevalent in recent years because of the efficacy of penicillin and the sulfonamides Occasionally serum is used in cases which are resistant to all other therapy The type of pneumococcus present must be known and the corresponding serum administered according to the following schedule

Certain precautions must be taken to prevent reactions due to horse serum sensitivity Antisera are not given to patients with congestive heart failure to those with positive sensitivity tests to animal serum, or a history of allergy Injection of 0 1 cc into the skin or administration of a drop or two of diluted serum into the conjunctival sac will reveal the presence of undue sensitivity within a half hour

Forty thousand units of serum may be given *intravenously* at once then 40 000 units every four hours for three or four doses In most uncomplicated early cases in young patients there is a rapid crisis after introduction of 50 000 to 100 000 units of serum Type II pneumonia requires more than twice this amount Dosage is increased with age if treatment was delayed if the pulmonary process is extensive if the patient is pregnant or bacteremic

Two important considerations in serum therapy are (1) Serum is given as early as possible that is within the first three or four days of onset but it may be used during any period if the patient is not *making satisfactory progress* (2) *the amount must be adequate* Small doses have no place in treatment

With the advent of refined sera the intensity and duration of serum sickness have been greatly diminished It usually begins about a week after serum therapy and is characterized by fever urticaria arthritis and lymphadenopathy in combination or alone The patient is kept in bed and given analgesics and codeine Immediate serum reactions include chill anaphylaxis sudden circulatory changes and miscellaneous reactions The chill is usually followed by a fever although the chill phase does not always occur Treatment is symptomatic Application of heat during the chill cooling drinks during the fever Usually symptoms disappear within a few hours but they may recur It is advisable to withhold further serum but if further serum therapy is necessary a different lot is used

Oxygen Oxygen insufficiency occurs in pneumonia because of the reduction of the tissues responsible for oxygen absorption Also there is a greater than normal demand for oxygen because of the fever and infection Cyanosis is usually a late evidence of oxygen want but one should not wait for cyanosis to appear before beginning administration of oxygen in pneumonia because oxygen therapy

seems to have other benefical actions When sustained rapid pulse and respiration cyanosis or delirium occur alone or in combination it is wise to start oxygen therapy

There are several ways of administering oxygen The older methods of using oxygen chambers or oxygen tents have almost entirely disappeared from practical work However the oxygen tent is valuable if the patient cannot tolerate oxygen given by mask or nasal catheter or if he does not receive adequate amounts by these methods This tent is more comfortable for the patient but it is also more expensive and very complicated for home use A full time nurse or other person trained in the use of oxygen therapy is necessary Analysis of tent air must be made every two or three hours to be sure that the patient is receiving enough oxygen If the patient requires a concentration above 60 per cent he should be exposed to it for only 24 to 36 hours or a high concentration may be given for 12 hours and then a lower concentration for 12 hours alternating this regime until treatment is no longer necessary

The Boothby mask for providing 100 per cent oxygen is a satisfactory method of administration Sometimes the nasal catheter is recommended for its simplicity and inexpensiveness With almost any method the patient should receive eight to ten liters of oxygen per minute Oxygen in the treatment of pneumonia appears to increase the oxygen saturation of the blood eases the distress caused by the lack of oxygen causes the patient to breathe more deeply and more effectively probably increases the circulation of blood in the lung and it is likely that it enhances the resistance of the patient against the pneumococcal infection Administration of oxygen should be continuous in a sufficient concentration 40 to 50 per cent by volume and discontinued gradually when it is no longer necessary If symptoms recur after oxygen withdrawal this treatment should be reinstated

Certain precautions are necessary in the room where oxygen is used Fire and highly inflammable materials are prohibited and lubricating oil must not be used on the equipment since high concentrations favor combustion To prevent irritation of the mucous membranes from the dry gas a vaporizing bottle should be used

The administration of positive pressure in conjunction with oxygen or helium oxygen mixtures and inhalations of vaporized solu

tions of neosynephrine and epinephrine may be beneficial One hundred per cent oxygen or helium-oxygen mixtures given under positive pressure tend to relieve the edema by preventing the exudation of serum into the lung and retarding the entrance of blood It is contraindicated only in shock Positive pressure is best administered by the helium oxygen hood and pressures of 1 to 6 cm water are maintained both in inspiration and expiration A mask in which the exhaled air passes out through a tube immersed in varying degrees of water may also be effective The flow of oxygen or helium oxygen should be from 7 to 10 liters a minute

Neosynephrine has a vasoconstrictor effect on the mucous membrane of the tracheobronchial tree and epinephrine is a bronchodilator Inhalation of vaporized solutions of neosynephrine and epinephrine is best done by passing five liters of oxygen from a high pressure tank through a nebulizer placed in 1 cc of one per cent solution of neosynephrine and 0 5 cc of 1 100 solution of epinephrine

Prophylaxis Prophylaxis consists of isolating the patient and careful disposal of secretions of the mouth and respiratory tract Contaminated articles must be burned or sterilized Since many cases of pneumonia are caused by healthy carriers or individuals convalescing from pneumonia who still carry the pneumococci in the respiratory tract carriers should be taught how not to pass the disease Sulfonamides have not done a great deal to reduce the convalescent carrier rate in pneumococcus pneumonia

INTERSTITIAL PNEUMONIA

(Primary Atypical Pneumonia of Unknown Etiology or Virus Pneumonia)

Interstitial pneumonia while a disorder bearing a resemblance to lobar broncho and influenzal pneumonia and other common respiratory diseases is distinguished from these in particular by the roentgenographic shadow

Etiology The acute interstitial pneumonias have been shown within recent years to be primarily nonbacterial in origin and of specific etiology namely virus or rickettsia Specific viruses (those of influenza and ornothotic pneumonic groups) have been demonstrated as the causative agents of interstitial pneumonias Primary atypical

pneumonia is thought to be caused by a filterable agent believed to be a virus however the entity still exists as primary atypical pneumonia of unknown etiology Specific rickettsial organisms such as those causing typhus, tsutsugamushi and spotted fever may during the course of the disease cause an interstitial pneumonia In an epidemic at Camp Patrick Henry Virginia caused by the rickettsia Burneti (the organism responsible for Australian Q fever) an interstitial pneumonia was demonstrated in over 90 per cent of patients

The interstitial pneumonias frequently cannot be separated clinically or roentgenographically without specific sera agglutinations The radiologic manifestations of the interstitial pneumonias are principally bronchitic peribronchitic and alveolar infiltrations singly or in combination In the epidemic of Q fever in addition to the above mentioned infiltrations a disseminated transitory focal type is described which suggests a hematogenous spread Occasionally the interstitial pneumonias may simulate lobar isolated bronchopulmonary segmental and bronchopneumonic consolidations all characteristic of the bacterial pneumonias Their differentiation can only be made by the clinical and laboratory methods Further the interstitial pneumonias not infrequently simulate incipient tuberculous infiltrations but the rapid resolution of these infiltrations and the absence of the specific acid fast organism aid in the differentiation with pulmonary tuberculosis Resolution of the interstitial pneumonias is rapid but infrequently it may be delayed beyond the clinical manifestations and only repeated roentgenograms will demonstrate the complete resolution over an extended period of time

Pathology The pathological findings are typical of hemorrhagic interstitial bronchopneumonia or acute bronchitis Adams and his associates in a study of two epidemics among infants found proliferation and sloughing of bronchial epithelium to be the most common finding The exudate in the bronchial lumen was primarily epithelial the main infiltrating cell was mononuclear Edema atelectasis and hemorrhage may occur The diseased epithelial structures of the lung often contain cytoplasmic inclusion bodies There are areas of deep red moist solidification in the lung with thickening of the interalveolar septa exudate in the alveoli and pus in the bronchi In some cases there may be enlargement of the spleen and

lymph nodes Microscopically these changes resemble those of acute follicular splenitis and mesenteric lymphadenitis

Signs and Symptoms The onset usually is insidious and the incubation period varies from ten days to two weeks Constitutional symptoms predominate over the respiratory one and an attack may follow exposure to cold dampness or upper respiratory infections Symptoms include malaise severe headache chilliness without rigor dry paroxysmal cough which becomes productive later low grade temperatures slow pulse Later in the disease coarse explosive rales may be heard and there is absence of dullness on percussion In severe cases dyspnea and asthmatic breathing may increase the dis comfort caused by the cough and the patient may become cyanotic However dyspnea and cyanosis are not common features of this form of pneumonia as the alveolar sacs of the lung continue to carry on their function fairly satisfactorily Coryza sore throat substernal pain photophobia dizziness anorexia nausea vomiting abdominal pain and diarrhea are all seen at times The duration of this dis order is usually from 4 to 14 days with a period of convalescence although there are cases which run for 6 to 8 weeks or even longer

The cerebrospinal fluid in patients with severe headache has been found to be sterile with normal cell count and protein content Blood counts and urinalyses are generally normal The leukocyte count and Schilling index may be decreased although white blood counts vary between 6000 and 9000 but may be as low as 3000 or as high as 15 000

The x rays reveal changes which are striking in comparison to the meager physical signs First the size of the hilar shadow is increased on one or both sides and then perihilar infiltration develops and the shadow spreads outward The infiltration is of a soft patchy or homogenous type and most dense near the hilus sometimes it resembles pneumonia A whole lobe is not usually involved Ordi narily a lower lobe is affected but in about ten per cent of the cases several lobes may be involved This picture is variable Lesions may disappear in a few days but they usually progress as described and recede slowly The x ray picture does not correlate the physical findings Roentgenographic changes may not be marked while the symptoms are most pronounced and often appear and progress while the symptoms are diminishing

There is a bronchitis resembling atypical pneumonia without the x ray findings and this may be a mild form of the same disease

Diagnosis The main diagnostic features may be epitomized as follows

1 Grippy sensations
2 Minimal physical signs
3 Characteristic x ray pictures
4 Normal white blood count or leukopenia
5 Irregular fever usually remittent
6 Sputum negative for pneumococci
7 No response to sulfonamides

Recently it has been discovered that cold agglutinins occur regularly in high titer in atypical pneumonia and usually not in other clinical entities This fact may be of importance diagnostically These agglutinins occur in dilutions of serum or plasma from 1 10 to 1 10 000 at 0 C (32° F) and the titers are highest at the end of the febrile period The height of the titers seem to parallel to some extent the severity of the illness

This condition may be difficult to differentiate from other types of pneumonia Other diseases which must be considered are tonsillitis colds nasopharyngitis known virus diseases as influenza and psittacosis fungus diseases pleurisy with effusion atelectasis cancer bronchiectasis and infectious mononucleosis Patients with pneumonia are generally more ill Laboratory identification of the etiological agent is important in the differential diagnosis

Prognosis The prognosis as a rule is good unless complications occur such as abscess formation or superimposition of pneumococcic pneumonia on the virus pneumonia However complications are rare

TREATMENT

Treatment is symptomatic All the usual supportive measures ordinarily employed in the management of patients with acute respiratory conditions are indicated Oxygen seems to be the most valuable therapeutic aid in severe cases

The place of sulfonamides in the therapy of virus pneumonia is disputed Some claim that they should not be used unless specifically indicated Others feel that since atypical pneumonia may be of pneu

mococcic origin sulfonamides should be given for the first three days If the patient is not benefited and it is proved that the infection is not pneumococcic the drug should be stopped at this time It is agreed that secondary infections must be prevented or combated and when these infections are susceptible to sulfonamides these drugs may be used to advantage Otherwise sulfonamides are useless and have no good effects in cases of uncomplicated virus pneumonia

Convalescent whole blood or serum may be useful However since virus pneumonia may be caused by so many different viruses it is hard to predict what would be the effect of these therapeutic agents in specific cases

The severe headache may be promptly relieved by lumbar puncture Or codeine sulfate 1/6 grain and acetysalicylic acid 5 grains may be given two or three times a day

Roentgen therapy in small doses between 35 and 90 r has produced cures in a few days With this therapy results are best when treatment is started in the early stages and not so good when started two weeks after the onset Roentgen therapy is especially effective in controlling the cough If it is taken in doses larger than those prescribed untoward results may occur However good effects have been obtained with 1 or 2 treatments of 112 r units each

Care must be taken to prevent the occurrence of secondary infections Since patients with virus pneumonia do not regain their strength quickly a long convalescence is recommended The average hospital stay is 27 to 34 days

Administration of positive pressure inhalations of helium oxygen mixtures and of vaporized solutions of 1 100 epinephrine and one per cent neosynephrine as for pneumonia may be beneficial

Sodium salicylate and sodium bicarbonate have been used for the generalized aches pains and fever

The value of penicillin is questionable but it should be used in cases which fail to respond to other treatment promptly

ACUTE FIBRINOUS PLEURISY

Pleurisy is an inflammation of the pleura Clinically it is divided into three types (1) Dry fibrinous pleurisy (2) pleurisy with effusion which may be serofibrinous purulent or hemorrhagic and (3) chronic pleurisy with thickening of the membrane

Etiology Pleurisy is seldom with certainty a primary disease it is usually a local manifestation of a systemic infection or a direct extension or complication of another lesion

The initial lesion is usually dry pleurisy which may or may not be followed by effusion The most common cause of dry pleurisy is an infection of the respiratory tract or the conditions which contribute to the latter It may also be caused by any inflammatory or neoplastic disease of the lung, or bronchiectasis

Pleurisy with serofibrinous effusion is commonly caused by tuberculosis Other causes are carcinoma, rheumatic fever trauma, jugular thrombosis, Hodgkin s disease, leukemia cirrhosis of the liver actinomycosis and parasitic infections

Purulent effusions are the result of infections caused by the pneumococcus and streptococcus, less often by the staphylococcus hemophilis influenzae and the Bacillus typhosus These pyogenic infections may arise in the lung in the mediastinum or below the diaphragm Empyema frequently begins as a simple serous exudate

Hemorrhagic effusions are caused by carcinoma of the lung or pleura by trauma and by streptococcal infections of the pleura

Chronic pleurisy with thickening of the membrane is the end result of the types described above

Pathology The pathology of pleurisy may be divided into several stages

1 The stage of hyperemia The membrane loses its luster and becomes dry and injected

2 Exudation of fibrin which upon coagulation gives a shaggy appearance to the membrane in dry pleurisy the process terminates here The fibrin covered surfaces adhere and the adhesions may obliterate the cavity Such pleurisy is well localized

3 Effusion The exudate is serofibrinous and yellow green to straw colored Floating flakes of fibrin may be seen The specific gravity varies from 1 010 to 1 020 The albuminous fluid coagulates on boiling The fluid may be hemorrhagic instead of simply fibrinous

4 The effusion may become purulent with predominance of polymorphonuclear cells Pneumococcal pleurisy is frequently purulent from the start

5 Resolution with variably extensive and variably permanent

adhesions This stage may be accompanied or followed by thickening of the involved pleural membrane

The effusion if extensive causes marked pressure on the lung tissue and viscera near it Atelectasis of a portion or sometimes the whole of a lung may ensue The heart and great vessels may be pushed to the opposite side The liver and spleen may be displaced downward

Signs and Symptoms The onset may be insidious or sudden Dry pleurisy is usually ushered in suddenly with lancinating pain on the affected side The pain is made worse by breathing or any movement of the involved region Dyspnea and lassitude are natural consequences of the pain The pain may be referred to the epigastric or umbilical region accompanied or preceded by chill and/or constitutional disturbances As effusion takes place the severe pain is replaced by more marked dyspnea The patient lies on the affected side to allow more freedom of motion in the sound lung Respiration and pulse are rapid and poorly productive cough is present with scanty mucoid sputum The sputum is never rusty unless pneumonia or other disease of the lung exists simultaneously Low grade fever may be present with dry pleurisy or pleurisy with serofibrinous effusion but when a purulent effusion appears the temperature usually rises abruptly and assumes a septic curve

The physical signs resulting from the fibrinous exudation are usually situated at the bottom of the axilla where the diaphragmatic and costal layers of the pleura are in close apposition The diagnosis is based upon a single physical sign which is a grating rubbing friction sound usually somewhat jerky and interrupted and often audible throughout the entire respiratory act The sound is described well by the French as the *bruit de cour neuf* The pleural friction rub at times is felt as well as heard The corresponding side of the chest is seen to be less mobile than its mate

Effusion changes the physical signs The friction rub disappears and is replaced by depressed absent or distant tubular breath sounds The corresponding side of the chest may remain relatively fixed The intercostal spaces may bulge if the effusion is large As a similar consequence the mediastinal structures may be shifted to the opposite side with corresponding change in their physical signs The area of effusion is flat to percussion Tactile fremitus is decreased or

absent Shifting dullness at times is demonstrated by altering the position of the patient An area of hyperresonance may at times be found above the level of the fluid on the corresponding side The presence of fluid is confirmed by the aspirating needle

In most of the cases of interlobar empyema so far reported the pus has been demonstrated in the fissure which runs along the vertebral border of the scapula when that bone is pulled as far forward as possible by crossing the arms in front The signs usually found in

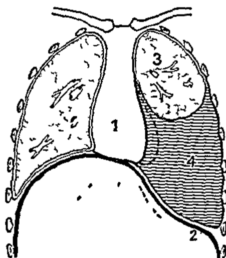


Fig 4—Left sided pleural effusion 1 Heart pushed over toward the right 2 diaphragm depressed (suppression of Traube s space) 3 left lung displaced upwards 4 effusion in pleural cavity

this condition are localized flatness on percussion diminished fremitus and feeble or absent breath sounds

The physical signs of pleural thickening are dullness to percussion to a variable degree diminished breath sounds, diminution or increase of voice sounds tactile fremitus and diminution of the normal respiratory excursion of the affected side

Diagnosis X rays of the chest usually confirm the presence of fluid in the pleural cavity Laboratory analysis of the fluid reveals a high lymphocyte count in serofibrinous effusions particularly those of the tuberculous group and a high polymorphonuclear count in the purulent effusion while tumor cells may at times be found in the fluid caused by neoplasm If the organism is not demonstrated on micro

scopic examination guinea pig inoculation may be necessary to establish the diagnosis Leukocytosis is usually present and with empyema it may be marked The sedimentation rate is usually elevated

Prognosis The prognosis of pleurisy depends entirely upon that of the disease with which it is associated Prompt and efficient treatment may improve the outlook

TREATMENT

1 It is very important that during the acute stages of pleurisy the patient rest in bed with plenty of fresh air until the temperature reaches normal and that later he resumes his active life slowly returning to bed in case fever recurs If tuberculosis is present treatment in a sanatorium is in order If accompanying the pleurisy there has been a change from a negative to a positive Mantoux test careful observation of the patient is necessary for 6 months to a year

2 Fixation of the chest usually brings relief To accomplish this a binder with shoulder straps is best during the acute stage In diaphragmatic pleurisy the binder should immobilize the upper abdomen as well as the thorax This type of immobilization is preferable as it can be easily removed and allows proper daily physical examination Later strips of adhesive tape about four inches wide long enough to extend beyond the mid line in front and back and applied during forced expiration are most satisfactory

3 For local relief of the pleuritic pain heat in the form of hot water bottles the electric pad or hot compresses may be applied

4 The above measures may fail to bring relief and if so the salicylates acetylsalicylic acid or phenylsalicylate in 0 33 Gm (5 grains) doses every two hours for four doses should be given In severe cases codeine sulfate 0 016 to 0 032 Gm (1/4 to 1/2 grain) every two hours or morphine sulfate 0 01 to 0 016 Gm (1/6 to 1/4 grain) hypodermically may be necessary

5 During the acute period while fever is present the diet should be that for all febrile conditions Some give six ounces of a liquid diet every two hours which may be sweet milk or buttermilk egg albumen fruit juices etc Perhaps the best guide to the food intake is the appetite of the patient The diet for months following the illness should be one of a high caloric and high vitamin content

6 The patient should drink plenty of water

7 The bowels should be kept open and regulated by use of a mild laxative as milk of magnesia 30 Gm (1 oz) every other day or cascara sagrada 4 0 Gm (1 dram) daily

In the treatment of serofibrinous pleurisy the binding of the affected side as a measure in an attempt to lessen the volume of effusion which collects seems to be a mistake as it may aid in the dislocation of organs and later hinder the absorption of fluid the latter being favored by deep respiratory movements

Counterirritation in the form of a mild mustard poultice application of tincture of benzoin or radiant light physical therapy seems to relieve the pain in serofibrinous pleurisy

In addition to medications as above calcium chloride or calcium gluconate is administered early in the disease in the hope of checking an increase of the effusion The rationale of this treatment is that fluid exudates can arise only in the presence of the sodium ion which in some degree the calcium displaces Frequent doses (6 to 12 per day) of a 6 6 per cent solution of calcium chloride (1 Gm or 15 grains of calcium chloride dissolved in 15 cc of water) are administered or two intravenous injections each week of 10 cc of a ten per cent calcium gluconate solution are given It is said this therapy has no effect after the effusion has collected or if the pleurisy is of the purulent type

Purulent effusions frequently require surgical drainage but this should not be done until frank pus has formed

The cause of any of the types of effusions must be sought and treated Extensive laboratory culture animal inoculations and frequent physical examinations may be required to make the diagnosis

INFLUENZA

Influenza is an acute highly infectious and contagious disease which occurs in endemic and epidemic forms with occasional pandemics It is characterized by an abrupt onset marked myalgia headache fever chills and prostration

Etiology The etiology has been variously thought to be a filtrable virus the Bacillus influenzae or both in symbiosis The causative organism is easily transmissible through secretions of the respiratory passages and is highly pathogenic The ages most affected are between 10 and 40 years Sex seems to possess little influence One

attack of the disease does not appear to confer lasting immunity

Pathology Involvement of the respiratory tract is characteristic Severe inflammatory injection of the upper respiratory mucous membranes is commonly found Bronchitis bronchiolitis tracheitis laryngitis and at times pneumonia are seen A serosanguinous exudate may be found in the air passages and there may be scattered areas of necrosis of the respiratory epithelium Lung findings indicate peribronchial inflammatory changes These changes occur early and if the patient survives are transformed to a purulent involvement bronchiectasis and chronic pneumonitis may result Pleural involvement was not common in the post World War pandemic If the central nervous system is involved there may be hyperemia of the meninges of the brain and cord

Signs and Symptoms The onset is sudden following a short incubation period varying from one to five days Fever ranging from 39° to 40 5° C (102 to 105 F) appears with chills or chilliness and marked prostration Usually catarrhal symptoms affecting the eyes nose and pharynx appear early and severe aching of the head back and extremities is characteristic The face neck and thorax may be flushed and tachycardia may be present Pharyngitis may be marked and a sense of soreness in the chest frequently accompanies it Gastrointestinal symptoms appear concomitantly with the respiratory complaints On the third or fourth day bronchitis of a purulent type associated with a productive cough manifests itself Auscultation may reveal many coarse or fine rales scattered through the lungs The temperature drops at this time to about 38 3° C (101 F) The cough is usually persistent chronic bronchitis frequently follows Sinusitis is often seen at this period and in children otitis media may be found

Pneumonia may accompany the involvement of the upper respiratory passages or be an immediate sequel to it The pneumonia is generally bilateral and the lower lobes are most often involved Fever is usually maintained and the tachycardia may continue Cyanosis and prostration are out of proportion to the pneumonic involvement Leukopenia is characteristic of the disease Recovery from such pneumonia is frequently delayed because of pulmonary complications as delayed resolution abscess chronic bronchitis or bronchiectasis

Diagnosis The following clinical signs may confirm a diagnosis of influenza Abrupt onset constitutional symptoms out of proportion to the physical signs fever and the absence of pneumonia During the acute phase of the disease either influenza A or B virus is recoverable from the throat washings thus isolating the influenza virus from the patient Another help in diagnosis is the demonstration of rises in antibodies to influenza in the patient s blood

Prognosis Endemic cases are usually mild and relatively few deaths result However in epidemics and pandemics there is a mortality of between 15 and 60 per cent The fatality rate rises with the second and third waves

TREATMENT

1 Isolation should be enforced to protect the patient from secondary bacterial invaders and to shield others from the disease The disease is usually only reportable during epidemics

2 Absolute rest in bed is essential until the temperature has been normal for several days and symptoms have disappeared This should be followed by a full week for convalescence before the usual routine is adopted Fresh air should be plentifully supplied

3 The diet should be soft or fluid Regular diet may be resumed as soon as the patient expresses a desire for food

4 Fluid intake should be adequate 3500 to 5000 cc daily during the febrile period Fruit juices are essential The patient should have a glass of fruit juice every hour he is awake

5 Headache and myalgia are combated by use of the salicylates Sodium salicylate acetylsalicylic acid or salol in 0 6 Gm (10 grains) doses with an equal amount of sodium bicarbonate given every two to three hours for four or five doses will usually bring relief In some instances small doses of codeine sulfate 8 to 30 mg (1/8 to 1/2 grain) repeated as often as necessary until the more intense pain subsides are indicated

6 At the outset of the disease a purge is advisable Magnesium sulfate 30 Gm (1 oz) or citrate of magnesia 1 bottle (200 cc) are satisfactory cathartics for this Afterwards the bowels should move daily with the aid of a mild cathartic or laxative as fluid extract of cascara sagrada 4 to 8 cc (1 or 2 drams) daily or a small tap

water enema Excessive catharsis in the asthenic or severely pros trated patient should be avoided

7 Relief for the congested nasal passages is secured by the local application of an ephedrine solution of camphor and menthol Mouthwashes irrigations of the throat and gargles should be regu larly employed Normal saline solution or dilute hydrogen peroxide is preferable for bathing the inflamed mucous membranes of the throat and mouth

8 Pain in the chest may be relieved by the application of a mustard plaster (one part mustard and three parts flour and warm water to make a paste and spread on muslin) The plaster should be left on the area for approximately 15 minutes

9 Repeated sponging is indicated for extremely high fever

10 Oxygen is always advised and if pneumonia supervenes it is necessary

11 The sulfonamides have not proved successful up to now

12 Vaccination against the disease has been tried but has not produced any striking reduction in incidence Its use is left to the discretion of the physician

The Lungs

(Continued)

ACUTE ASTHMA

Asthma is a disorder characterized by hypersensitivity to some foreign substances which are taken into the body by eating inhalation injections infections absorption from chemical or other toxic agents and sometimes by an autointoxication associated with toxic conditions within the body Paroxysmal attacks occur at variable intervals and are commonly seen in several members of a family or in a family where other members are suffering from allergic diseases

Signs and Symptoms The attacks may be mild characterized by wheezy breathing for a short period of time or severe at times appearing to threaten the life of the patient The distinguishing feature of such an attack is the difficulty in expiration and the lack of any disturbance of the inspiratory phase of breathing In heart disease laryngismus stridulus and foreign bodies the breathing difficulty is of inspiratory kind rather than expiratory

Diagnosis The diagnosis of bronchial asthmatic seizures is not difficult as the dyspnea is almost always expiratory Examination reveals the characteristic dry rhonchi sibilant and sonorous over the entire chest A careful examination of the heart usually is sufficient to rule out heart disease as the cause of dyspnea In cardiac asthma the engorgement of the lung is produced by over distention of the pulmonary vessels and the rales are of the moist type it is pulmonary edema that characterizes the clinical picture In bronchial asthma the lungs are dry The most striking feature of the patient in the seizure of bronchial asthma is the superficial type of respiration of the expiratory variety

TREATMENT

While an attack of bronchial asthma seldom endangers the life of the patient it does so occasionally It always causes the patient distress and relief is more than welcome

1 When called to see a patient in an asthmatic seizure one

should administer 0 5 cc of 1 1000 solution of adrenalin (epinephrine) subcutaneously for immediate relief This dose may be repeated every hour or two or oftener if needed but it is seldom necessary to repeat it more than once or twice A nasal spray of a solution of 1 100 epinephrine augments the action of the subcutaneous dose Adrenalin should not be given to children in injections of more than 0 12 to 0 18 cc (2 or 3 minims) and the injection should be given subcutaneously only This dose may be repeated in 20 to 30 minute intervals If adrenalin does not work in the first few doses the drug should not be used Prolonged adrenalin medication is not recommended as the drug is habit forming the dosage cannot always be controlled and abdominal crises may ensue

2 Ephedrine 0 05 Gm (¾ grain) may be given orally four times a day Ephedrine is not as effective as epinephrine in controlling a severe attack but is decidedly beneficial in preventing a mild dyspnea from growing worse When applied locally to the mucous membranes it is less irritating and produces a more lasting constriction than does epinephrine

3 If adrenalin does not relieve an attack the asthma is probably due not to bronchiolar spasm but to bronchial edema with bronchial plugging Syrup of ipecac should be given in these cases ½ to 1 teaspoonful for infants and young children and more for older children to induce vomiting If the ½ to 1 teaspoonful dose does not cause the infant or young child to vomit two teaspoonfuls may be given The ipecac should be followed with warm water

If the attack is prolonged the ipecac should be followed by the administration of 10 to 15 per cent intravenous glucose given by slow drip infusion (300 cc for young children and 500 to 1000 cc for older ones) One one thousandth of adrenalin may be mixed in with this infusion to make a dilution of 1 300 000 to 1 1 000 000 This prevents or helps dehydration and may relieve edema

4 Morphine is contraindicated If sedation is necessary it must be obtained by using sodium phenobarbital 0 033 Gm (½ grain) subcutaneously or paraldehyde 15 to 30 cc (½ to 1 ounce) per rectum This is dissolved in 60 cc (2 ounces) of some oily substance as olive oil Other acceptable sedatives include bromides 0 66 to 1 Gm (10 to 15 grains) and chloral 0 12 to 0 42 Gm (2 to 7 grains) which may be given intravenously Triple bromides 0 33 to 1 Gm

(5 to 15 grains) amytal 0 033 Gm (½ grain) and/or acetyl salicylic acid 0 33 to 0 66 Gm (5 to 10 grains) may be given orally This sedation may be repeated in two or more hours

5 Aminophylline 0 5 Gm (7½ grains) in 50 cc of 50 per cent glucose solution intravenously often but not always controls the seizure If relief is not afforded the addition of 0 5 cc of adrenalin 1 1000 solution to the intravenous solution may produce striking effects When adrenalin aminophylline and hypertonic glucose are ineffective ether 30 cc (1 ounce) in 60 cc (2 ounces) of olive oil given rectally is useful in controlling status asthmaticus

6 Sometimes in severe cases intravenous normal salt solution usually containing five per cent glucose is beneficial The dose should be large 1500 cc or more and given quite rapidly Solutions of hypertonic glucose 100 cc of 50 per cent solution given daily for two or three days are also recommended

7 Oxygen and helium either alone or in combination when given through a nasal catheter may promote comfort It is not usually well to give oxygen therapy in a tent as this may upset the patient Asthmatics are likely to experience claustrophobia during attacks

8 The inhalation of fumes from burning asthma powders which contain stramonium leaves and potassium nitrate may afford temporary relief in mild attacks

9 Whenever the attack is prolonged and the above measures have failed the patient should be moved to different surroundings Removal to a different room and bed or to a friend s house near by is often quite effective Extrinsic causes can usually be avoided by removal to a clean hospital bed

The general management and prevention of recurrence of attacks consists in the determination and exclusion of the exciting substance (allergen) which may be discovered experimentally or through cross examination of the patient If an offending allergen is found the simplest and most satisfactory method of treatment is the prevention of contact by the patient with the excitant If this is impossible then desensitization therapy through the injections of specific or nonspecific proteins may be instituted The failure to determine a cause calls for further physical examinations looking for infected teeth or tonsils gall bladder disease anomalies or dis

eases of the nasal passages and sinuses and complete study of the gastrointestinal tract

The selection of drugs for administration during the free period is difficult but the iodides sodium or potassium in doses of 0 33 Gm (5 grains) three times a day is recommended A ten per cent solution of calcium chloride in doses of 15 cc (½ ounce) three times a day occasionally has a good effect Calcium has no place in the treatment of the acute paroxysm however Benadryl often relieves vasomotor rhinitis but has little effect on the asthma itself Pyribenzamine a closely related compound 50 mg four times a day after meals has also been used

Physical agents as roentgen ray therapy diathermy actinotherapy and hydrotherapy have their proponents but results of this treatment are unreliable and temporary in their benefits

Surgical measures as extirpation of sympathetic ganglia or section of the vagus in the cervical region have been attempted in the belief that the number of constricting stimuli to the bronchi are reduced Bronchoscopic lavage and local therapy in the bronchi have been found of value in nonsensitive cases with profuse expectoration and a chronic tracheobronchitis The benefit of surgical procedures however is usually transitory

The administration of endocrine substances such as thyroid ovarian extracts and parathormone has proved effective in certain cases Change of climate is advantageous in many cases Breathing exercises are recommended Psychic therapy has its place in certain selected cases In the case of an asthmatic patient the physician must be aware that he is treating a constitutional disease and steps must be taken to correct any abnormalities or local or systemic diseases impairing the health of the patient

SPONTANEOUS PNEUMOTHORAX

Pneumothorax or air in the pleural cavity may be of two types (1) the spontaneous kind which arises from the rupture of emphysematous blebs and from perforation of the pleura by carcinomatous tuberculous and other destructive lesions or (2) the artificial form which constitutes the introduction of air into the cavity for therapeutic purposes Spontaneous pneumothorax is characterized by its abrupt

(5 to 15 grains) amytal 0 033 Gm (½ grain) and/or acetyl salicylic acid 0 33 to 0 66 Gm (5 to 10 grains) may be given orally This sedation may be repeated in two or more hours

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the chest deviated or absent apical heart beat limited chest movements and widened and bulging interspaces Breath sounds are usually absent on auscultation though tinkling rales may be heard occasionally Peculiar amphoric sounds with a metallic ring are often detected when the patient coughs Percussion reveals hyper resonant or tympanitic tone but this may be dull if pressure within the pleural cavity is high If the valve like opening is patent a typical cracked pot sound is heard Vocal fremitus is diminished or absent Palpation may reveal an air-cushion sensation over the interspaces There is absence of respiratory mobility of the lower lung margin with dullness in this area In left sided pneumothorax the heart may be displaced to the right or cardiac dullness may even be obliterated The coin test reveals a peculiar sound

Air may escape into the mediastinum and along the pericardium When this occurs auscultation along the left border of the sternum may reveal a peculiar crackling sound coincident with each beat of the heart This is known as Hamman s sign and is diagnostic of mediastinal emphysema

The course of spontaneous pneumothorax is dependent on the perforation Usually the pneumothorax becomes stationary when enough air enters the pleural cavity to overcome the negative pressure Sometimes the opening has little tendency to close and the collapse will remain stationary for a rather long period of time and then reexpansion takes place very slowly In other cases the opening closes almost immediately and the lung expands in a few days or weeks

Diagnosis This acute type of lung collapse must be distinguished from heart disease as coronary thrombosis and acute pericarditis and from other lung diseases as massive collapse pulmonary embolism and infarction and pleurisy Sometimes rupture of a large emphysematous bulla in the hilar area may simulate pneumothorax Pneumonia and diaphragmatic hernia also must be kept in mind

X ray examination and aspiration of air after paracentesis help in arriving at the correct diagnosis Sometimes a pneumothorax and a large peripheral cavity may seem alike on x ray examination but usually the pneumothorax is in the lower part of the chest while the cavity is apical The chest wall is generally retracted in cavities but bulging in pneumothorax

onset in apparently healthy persons usually young adults It almost always clears up uneventfully

Etiology Kjaergaard has endeavored to explain the rupture of emphysematous blebs or subpleural valve vesicles by (1) Localized emphysematous changes in the lungs (2) scar tissue in the lungs and (3) congenital cystic disease of the lungs Another suggested cause is rupture of the mediastinal pleura in the presence of mediastinal emphysema Years ago the cause of spontaneous pneumothorax was believed to be rupture of a tuberculous focus or some other destructive lung process piercing the pleural cavity Recently however it has been noted that pneumothorax occurs most often in people who are free of demonstrable disease and the cause in these instances is given as rupture of blebs near a pulmonary scar or of an emphysematous bleb It has been proposed that a congenital pleural defect or a constitutional inferiority of the pleural structure may cause pneumothorax or the formation of pleural blebs Since emphysema is a disease of later life pulmonary emphysema may be excluded as an etiological factor as a general rule Spontaneous pneumothorax occurs most often among young adult males suggesting a constitutional factor in the causation It has also been noted that it occurs in families Chest trauma or mechanical strain are also common causes of the disease If a pulmonary infarct is septic it may break down and allow free air to pass into the pleural cavity resulting in pneumothorax

Signs and Symptoms The earliest and commonest symptom of spontaneous pneumothorax is sudden pain at the time of rupture with or without collapse The pain involves the entire side of the chest shoulder back or substernal area However this symptom need not be present and often the patient is not at all conscious of his condition and it is discovered incidentally Often the patient is heart conscious because of dyspnea of varying degree Marked pallor is noted Cyanosis and a sudden rise in temperature is a common finding in children but usually is lacking in adults Respirations are shallow and rapid The pulse is small and fast and in very severe cases syncope and collapse may ensue with a subnormal temperature A dry unproductive cough is often an accompanying feature of the disease

Physical findings include increased size of the affected side of

the opposite side or alternating A sterile pleural exudate should be produced in these cases by injecting *substances into the pleural sac*

10 Bilateral pneumothorax may occur if the strain of compensating for the involved lung is too great on the opposite one Emergency aspiration of air and oxygen is necessary

11 If hemorrhage from the torn lung into the pleural space (*hemopneumothorax*) takes place measures to combat shock must be instituted Sedation blood transfusions plasma parenteral fluids and oxygen are indicated

HEMOPTYSIS

Coughing or spitting of blood is always a serious sign In the strict sense hemoptysis means expectoration of blood from the lungs or bronchi with the exclusion of blood from the nose or throat This *bleeding from the lungs or bronchi usually results in the spitting of* bloody sputum though conditions associated with bloody sputum do not always cause hemoptysis

Etiology Hemoptysis is most commonly produced by pulmonary infarction pulmonary *tuberculosis and other acute inflammatory* lesions abscess or gangrene of the lung carcinoma of the lung bronchiectasis ulceration of any part of the respiratory tract or mitral stenosis though there are many other causes It is also a symptom in some hemorrhagic or blood diseases and frequently occurs with trauma as gunshot or stab wounds foreign bodies and contusions

Diagnosis The diagnosis of hemoptysis is not very difficult though it may be confused with hematemesis There is usually a history of pulmonary or cardiac disease in hemoptysis while in hematemesis the history is of a gastric disturbance In hemoptysis the blood is coughed up mixed with sputum and is frothy and bright red and alkaline in reaction in hematemesis it is vomited *clotted and acid in reaction After the first spell of hemoptysis* the patient usually coughs up dark clots of blood for a day or two

Prognosis The bleeding in hemoptysis is seldom extensive or persistent From rupture of mycotic aneurysm of a lung vessel a large tuberculous cavity *or perforated aortic aneurysm* hemorrhages may be copious An opinion prevails that hemorrhage from mitral heart disease is usually small and insignificant Such hemoptyses may result from a ruptured or distended engorged blood vessel from rupture of a

Prognosis Generally speaking the prognosis is excellent although attacks often recur in about 25 per cent of cases Emphasis must be placed on complete recovery as patients will then be spared undue worry

TREATMENT

1 The patient should be put to bed immediately and kept there for at least two weeks A half sitting position is preferable Complete bed rest for patients with partial pneumothorax will prevent a total collapse All these patients should have restricted activity for a year

2 The patient should be given a diet rich in calories and vitamins

3 Morphine sulfate 0 01 to 0 016 Gm (⅙ to ¼ grain), hypodermically or codeine sulfate 0 03 to 0 06 Gm (½ to 1 grain), administered orally or hypodermically may be given as needed to relieve pain and control the cough

4 Sedatives as phenobarbital 0 03 Gm (½ grain) three or four times daily or sodium bromide 1 Gm (15 grains) or chloral hydrate 1 Gm (15 grains) daily are indicated for sleeplessness

5 Oxygen administration is of value and some authors feel that by inhalation of 100 per cent oxygen apprehension strained effortful breathing and pain may be relieved There is also evidence that pure oxygen inhalation aids in absorption of the spontaneous pneumothorax since oxygen displaces the nitrogen present in the pneumothoracic space

6 Some advise that the affected side of the chest be strapped in order to prevent any chance of forced respiratory movements reopening the fistula and to forestall progressive distention of the affected side

7 If the heart is displaced thoracentesis with withdrawal of small amounts of air is advisable

8 In tension cases patients should be kept in bed for three or four weeks Small quantities of air should be removed repeatedly In most cases sedation should be continued and no attempt made to lower the intrapleural pressure until the perforation is well sealed Reexpansion usually takes place in six to ten weeks if tuberculosis is suspected reexpansion should be delayed by the injection of air

9 Recurrent attacks may occur involving either the same side

cases of small repeated hemorrhages by mouth in amounts ranging from 1 to 3 Gm (15 to 45 grains) four times a day

5 Small multiple transfusions (50 to 75 cc) of citrated blood have proved a valuable aid but the necessity of securing a suitable donor cross matching and typing of the blood militate against the use of transfusions during the acute episodes

6 Vitamin K 5 mg intramuscularly may be given

7 Blood coagulants as hemoplastin or fibrinogen may be given

8 Inhalation of amyl nitrite may be of value

9 After the hemoptysis is under control determination of the cause of the bleeding must be sought

ACUTE MILIARY TUBERCULOSIS

Acute miliary tuberculosis may be defined as an acute form of tuberculosis in which minute tubercles are formed in a number of organs due to dissemination of the bacilli throughout the body by the blood stream

Etiology This disease is commoner in childhood and the adolescent period of life than in after years but it may occur at any age The tubercle bacilli which cause the formation of tubercles diffusely spread throughout the lungs and other organs arise from a focus in the lung or the abdominal cavity or from an old tuberculous focus in some bone joint or other part of the body Usually the patient has had a tuberculous lesion which has undergone healing Then he has an acute infectious disease and the old focus is relighted and the tubercle bacilli are poured into a vein carried to the heart and disseminated throughout the organs

Pathology The organs usually are covered by tubercle bacilli which are carried to the bronchial arteries by either the greater or the lesser circulation the pulmonary arteries or both The bronchial arteries favor a more uniform distribution of tubercles within the stroma of the lungs

Signs and Symptoms Acute miliary tuberculosis may be classified into the following forms

1 Generalized
2 Pulmonary
3 Meningeal

mycotic aneurysm or from pulmonary infarction In cases of ruptured aneurysmal sac, bleeding may be copious prolonged and fatal

TREATMENT

Hemorrhage due to tuberculosis must be treated carefully so that the tuberculosis is not scattered Morphine is effective in reducing fear and coughing but in tuberculosis it must be used cautiously or the infected blood will not be expectorated and the tuberculosis will spread Profuse and repeated bleeding calls for artificial pneumothorax but before this can be done the physician must determine which side is bleeding Sometimes pleural adhesions are present and thus pneumothorax is prevented

Serum injections pituitary extract atropine calcium and the nitrites have been used in the treatment of pulmonary bleeding Treatment consists in stopping the hemorrhage and preventing its recurrence An injection of morphine should be given for profuse bleeding but care must be taken so it does not stop the coughing and consequently the expectoration since the patient might suffocate if the bronchial tubes were filled with blood

The immediate treatment consists of

1 Absolute rest in bed in a semirecumbent position The anxiety of the patient should be allayed by assurance that the amount of blood lost is trivial that the bleeding will soon cease and that death from hemorrhage is rare

2 Nothing is given by mouth except ice chips for 36 hours after which only liquids and semisolids should be given

3 Cold compresses should be applied to the head neck and chest over the heart

4 If the hemorrhage is profuse morphine sulfate 0 01 Gm to 0 016 Gm (1/6 to 1/4 grain) hypodermically may be administered as necessary to secure absolute quiet This drug must be used cautiously in tuberculosis Other drugs which may produce a beneficial effect are Sodium amytal 0 2 Gm (3 grains) repeated as often as necessary to secure quiet in less severe cases atropine sulfate 0 0003 to 0 0006 Gm (1/200 to 1/100 grain) given hypodermically every 4 hours emetine 0 05 Gm (3/4 grain) hypodermically three or four times a day and calcium chloride (20 cc of a 15 per cent solution) intravenously Calcium gluconate or calcium chloride may be given later or in

tubercle bacilli in the sputum but x ray examination of the chest usually is relied upon for correct diagnosis A diffuse speckling is found throughout both lungs and the picture is usually characteristic of tuberculosis

3 Meningeal Miliary Tuberculosis In tuberculous meningitis the invasion of the meninges by tubercle bacilli gives rise to a typical tuberculous inflammation of the pia mater The tubercles coalesce and form caseated tuberculous nodules The exudate practically never becomes purulent but is fibropurulent in character and may be quite clear One of the chief changes especially in younger individuals is the accumulation of fluid in the ventricles of the brain which are usually distended and often lead to what is called acute hydrocephalus

The symptoms of acute tuberculous meningitis may be divided into three stages corresponding to practically three weeks of the disease

(*a*) *The Prodromal Stage* In this period the patient is irritable and apathetic but there is no definite physical sign that identifies the condition Headache general malaise and a rise in fever to 37 8 C (100 F) mark the onset of the condition Loss of appetite weakness nausea and tachycardia are also typical features This period characterized by indefinite symptoms usually lasts a week or ten days

(*b*) *The Stage of Irritation* The headache becomes more severe and rigidity of the neck sets in The temperature is more intermittent Vomiting delirium and signs of intoxication are more marked The pulse may be irregular and slow at one period and very rapid and regular at another This period may also last a week or ten days

(*c*) *The Paralytic Stage* The final phase of the disease is ushered in by collapse convulsions and paralysis of some of the cranial nerves Coma may develop at this time and death may take place in from four to six weeks after the very beginning of the disease Cerebral vomiting delirium stupor and convulsions may come and go during this final phase of the disease

Diagnosis Although the clinical picture is quite characteristic one cannot rely on these indefinite findings alone to make a diagnosis A lumbar puncture reveals cerebrospinal fluid which is under great

1 **Generalized Miliary Tuberculosis** The onset of this form may be insidious and the patient may be free from severe symptoms Grippe acute bronchitis or a simple upper respiratory infection may usher in the first phase of the disease A past illness of tuberculosis should be kept in mind because the simpler kinds of infections may light up an old apparently healed lesion Weakness loss of appetite and fever characterize the first phase of the disease Rapid pulse dry tongue headache and an afternoon rise in temperature usually develop This form of miliary tuberculosis is often called the typhoid type because the spleen liver mesentery and intestines are usually studded with tubercles The focus is usually a broken down lymph gland which lies adjacent to a vein leading to the main pulmonary vein The tubercle bacilli flow into the left chambers of the heart and are spread throughout the body

The most important features of this type of miliary tuberculosis are the irregular fever and the slow insidious onset with gradual but persistent downward trend Leukocytosis or leukopenia may be present Differential blood count as a rule reveals a very decided rise in the stab forms Later lymphocytosis may occur but it is not seen in the earlier phase As the kidney may be involved in this process the tubercle bacillus may be found in the urine Since this disease may be confused with typhoid numerous agglutination tests should be done Other diseases as undulant fever certain types of syphilitic infections and some acute infectious diseases as acute endocarditis usually have to be considered in the differential diagnosis Special blood tests as well as blood cultures must be done to facilitate the diagnosis

2 **Pulmonary Miliary Tuberculosis** The tubercle bacilli are poured into the right side of the heart from the bile duct or from blood borne from outside the thoracic cavity These bacilli are then disseminated throughout the lungs

The onset is usually sudden with severe cough dyspnea and cyanosis The amount of sputum may be negligible Fever is a marked feature rising to 40 C (104 F) at times The physical examination shows very little evidence of pulmonary damage On auscultation there may be many rales scattered throughout both lungs The disease may be simulated by bronchitis influenza or bronchopneumonia The diagnosis is usually clinched by finding

General Measures

1 A fluid or light diet may be given with careful attention to its digestion assimilation and excretion

2 In typhoidal forms tepid or cool water or alcohol sponge baths reduce the fever and add greatly to the comfort of the patient

3 For relief of cerebral symptoms the ice cap systemic sedatives and narcotics are indicated

EDEMA OF THE LARYNX

Etiology Acute edema of the larynx (edema of the glottis) may develop as a complication of a constitutional disorder as in acute or chronic nephritis and heart failure or it may be a sequel to pressure from tumors of the thyroid or the larynx It is usually not a serious matter when there is merely an edema of the larynx Actually the term edema of the glottis should be limited to those cases in which an inflammatory lesion from some infection extends to and involves the entire larynx In these cases not only the glottis but the entire larynx is inflamed and swollen and closure of the larynx endangers the patient s life

Signs and Symptoms Edema of the larynx is rarely primary but it may follow a large variety of diseases The symptoms usually set in abruptly At first the patient feels some difficulty in breathing or swal lowing and rapidly a sense of suffocation develops Soon the patient is unable to speak and cyanosis of the neck and face follow The distress ful breathing due to the stenosis of the larynx becomes stridulous The sense of suffocation makes the patient anxious and this anxiety added to the lack of air causes him to become almost hysterical at times

Diagnosis The diagnosis of the condition is not usually very diffi cult The patient as a rule has been having sore throat laryngitis sep tic pharyngitis infection of the glands of the neck erysipelas or some other infection about the neck or throat Once a physician sees a patient with edema of the larynx in a paroxysm of stertorous breath ing cyanosis of the face and neck paroxysms of coughing in an at tempt to dislodge the obstruction he probably will never forget it The patient s futile attempts to save himself from strangulation and the anguish of the helpless and terror stricken onlookers present an unforgettable experience If there is any doubt about the diagnosis

pressure usually over 250 mm of water This fluid is as a rule fairly clear and not turbid as in septic meningitis Then too there is a lymphocytosis rather than a polymorphonuclear leukocytosis as in other kinds of meningitis It is always wise to attempt to find the tubercle bacilli in the so-called veil that forms in this clear fluid if it is allowed to stand in a test tube overnight However it is sometimes a difficult and tedious task to isolate the tubercle bacilli from the spinal fluid of these cases

Prognosis Prior to the advent of streptomycin acute miliary tuberculosis regardless of type was generally conceded to be a fatal disease Since the advent of streptomycin therapy authentic recoveries have been reported Prognosis is governed by the duration of the disease prior to therapy and also by the presence of central nervous system involvement The earlier the case the better the prognosis In those patients in whom meningitis is present together with the generalized miliary tuberculosis results with streptomycin therapy *have been disappointing In miliary tuberculosis where the spinal fluid cultures are negative and clinically there is no involvement of the central nervous system results with streptomycin therapy are very encouraging*

TREATMENT

The main objective of therapy is to control the symptoms in an attempt to make life more comfortable for the patient This is done by repeated lumbar punctures for the relief of the increased intracranial pressure Treatment of miliary tuberculosis may be divided into specific and general measures

Specific Measures

1 *Treatment is best carried out in the sanitorium* since a period of about six months is needed for cure

2 *Streptomycin in dosage of 2 Gm (30 grains) daily* is usually given Even in those cases where meningeal involvement is present streptomycin should be used in the possibility not only that a cure may be affected but that relief of the distressing symptoms of the meningitis in the early cases which is usually dramatic may occur

3 Para amino salicylic acid and promine have been used in conjunction with streptomycin therapy Whether or not the efficacy of streptomycin alone is enchanced is equivocal

5 After the emergency is over and the patient is breathing nicely again the less important phases of the operation as ligating any bleeding points obtaining a proper type of tracheotomy tube stitching up the skin and subcutaneous tissues and applying antiseptic solutions should be carried out

6 Finally it must be emphasized that an emergency tracheotomy is a lifesaving measure and when it is indicated it must be performed promptly without tremor or fear Every physician and surgeon whether internist or specialist should be able to perform this emergency operation

Minute details of the operation which are necessary and required in an operating room must be for the most part forgotten for the moment and attended to later on in an emergency It is better to have a live patient operated on under conditions where there is lack of sterility and exacting surgical technic than to have the patient dead as the result of waiting for someone to come with the proper implements of precision and the proper surgical training to perform the operation with scientific correctness Good advice for every physician is to carry an emergency kit which is within easy reach and contains very simple medicines and instruments so that these dire emergencies may be handled and a life saved without too great a delay

FOREIGN BODY IN THE RESPIRATORY TRACT

If a foreign body enters the respiratory tract below the epiglottis the patient s life may be in danger A variety of foreign bodies may block the windpipe The commonest kind consists of pieces of food which lodge in the windpipe during the act of swallowing when it is suddenly interrupted by laughing coughing or crying At these times slippery fruit stones or hard particles of food may be sucked into the upper respiratory tract While these emergencies arise more commonly in children they may occur in people of any age Obstruction by foreign bodies in the lower respiratory tract is often encountered among older individuals and especially in apoplectic patients If fluids pass down into the respiratory tract they are often successfully coughed up but if the reflex mechanism of coughing is abnormal owing to some disease then aspirated liquids may not be thrown out and they may cause death If a solid body of any kind

and one cannot see edema around the epiglottis one's *suspicions may be confirmed by inserting the index finger into the pharynx where he will feel the swollen tense, and turgid epiglottis*

TREATMENT

There is *little time* for procrastination in the *management of a* case of edema of the larynx Mild cases may pass over *quickly, but severe ones require daring procedures* In mild cases *adrenalin solution* of 1 1000 may be sprayed into the throat A *sedative, as pantopon* 0 02 to 0 01 Gm (⅓ to ⅙ grain) should be *administered to* allay the anxiety of the patient In the more *severe cases* it may be *necessary* to mechanically raise the epiglottis *with a forceps* and if the condition does not subside rapidly there should be no *hesitation in performing* a tracheotomy at *once*

The emergency tracheotomy may be done in a number of ways *but the following procedure is best*

1 The thyroid cartilage is located and *the cricoid cartilage is readily* felt One should paint the area below and *around the cricoid* cartilage with iodine or alcohol quickly

2 A sharp scalpel or a razor blade in an *emergency is quickly* disinfected with carbolic acid alcohol or *any antiseptic solution*

3 A *longitudinal* incision about an inch long *is made over the* upper part of the trachea below the cricoid cartilage It *should be* emphasized that sterile *precautions should* be observed as fully as possible but *in dire emergencies the main thing* is to open up the windpipe so the patient will *not suffocate* Then the skin and subcutaneous tissue are retracted *Bleeding* must be *controlled* as fully as possible by pressure or if one has the instruments by a clamp or two

4 The tough cartilagenous trachea is felt and with the sharp *instrument* a longitudinal incision *of one half inch or more is* quickly *and daringly* made The lips of *the incised trachea must be* separated *with a forceps* if it is available *or with some blunt instrument* which has been *sterilized* and the aperture *in the trachea should* be kept open *until* a regular tracheotomy tube or an *improvised one* as a short *piece* of hard rubber *tubing* can be inserted It must be emphasized that a safety pin must be attached to the tube so it will not *slip from the operator's fingers* and go down the windpipe

and frequently by collapse The involved side may be painful but usually is not Fever rises soon after the onset however it may be entirely absent Blood pressure may drop 10 or 15 points on the systolic side When an entire lung is collapsed coughing and bloody sputum are less apt to be present In cases of partial collapse the symptoms of cough and hemoptysis are more prominent The leukocyte count varies from 10 000 to 20 000 It must be kept in mind that pneumonia collapse of the lung and pulmonary infarct may occur in the same individual

Diagnosis Massive collapse involving a whole lung may be entirely overlooked because the symptoms may be meager The chief identification marks may be listed as follows

1 The sudden onset of dyspnea is characteristic Sometimes it is mild and brought on by exertion while at other times it is urgent and present without exertion

2 Cough and expectoration are usually present

3 Cyanosis may be mild or severe depending on the condition of the other lung

4 On physical examination the chief sign is the displacement of the heart to the collapsed side The collapsed side is shrunken and the spaces between the ribs are greatly narrowed

5 Movement of the collapsed side is hardly present The tactile fremitus over the collapsed lung is gone

6 The percussion note is greatly impaired as in a consolidated lung

7 Auscultation over the collapsed lung usually reveals tubular breathing as found in lobar pneumonia but breath sounds may be absent

8 The patient may cough up a large quantity of gelatinous sputum containing blood This may not occur until the disease has existed for several days and expectoration may be followed by inflation of the lung

9 X ray examination will practically always clinch the diagnosis the displacement of the heart in the direction of the collapsed lung and the elevation of the diaphragm on the collapsed side are almost sufficient to make a final diagnosis of massive collapse

In addition to the specific characteristics of massive collapse of the lung these patients may be suspected of having pneumonia pul

becomes lodged below the larynx, death may occur unless something is done immediately

The effect of foreign bodies may be two fold (1) That of obstruction to the passage of air, and (2) that of damage to the mucous membrane of the tube itself Abscesses pulmonary edema and gangrene may develop as remote effects of obstruction

TREATMENT

The treatment depends upon the grade of obstruction produced by the foreign body

1 If the obstruction is quite complete no time is to be lost before obtaining relief This means an immediate tracheotomy with removal of the foreign body if it can be located

2 If the condition is not quite so urgent a bronchoscopist or any one with the ability to insert the bronchoscope should be called and the foreign body removed with this instrument

MASSIVE COLLAPSE OF THE LUNG

Etiology Massive collapse of the lung is usually a complication of some other disease The conditions which most commonly are followed by complete atelectasis are (1) surgery (especially upper abdominal operations) (2) trauma to the thorax, (3) foreign body in the bronchus or trachea and (4) bronchogenic carcinoma Massive collapse comes on within a few hours to three days after an injury or operation especially one requiring general anesthesia Some other conditions which precede massive collapse are diphtheria pregnancy edema of the glottis, influenza and vagal stimulation causing constriction of the bronchus Massive collapse occurs when a main bronchus is obstructed occlusion of a secondary bronchus is followed by lobar atelectasis and of a smaller bronchus by patchy atelectasis Incomplete obstruction may bring on emphysema Predisposing factors in atelectasis are diminution in the depth of respiration and loss of the efficiency of the cough reflex The most important factor in this disorder is lowering of the tonus of the respiratory muscles which decreases intrathoracic volume and respiratory excursions This loss of tone may be due to anesthesia or psychic shock

Signs and Symptoms The manifestations of this condition begin abruptly and are characterized by dyspnea weakness tachycardia

Etiology Lung abscess is caused by pneumonia or other infections of the lung tissue with suppurative anaerobic microorganisms The primary focus of infection may be an oral abscess tonsillitis or pyorrhea Pulmonary abscess is caused by the inhalation of organisms with or without the association of the ordinary pyogenic organisms Conditions which favor the entrance of these organisms from the upper air passages especially operations as tonsillectomy or tooth extraction favor the development of an abscess through the aspiration of infected blood

Inhalation of foreign bodies is a frequent cause of pulmonary abscess especially in children These foreign bodies may cause partial or total occlusion of a bronchus with consequent edema in the area distal to the occlusion and often atelectasis this latter condition offers a most favorable opportunity for bacterial infection Oily substances introduced into the nose in the form of nasal drops or sprays occasionally gain entrance into the pulmonary tissue by way of the bronchi and give rise to lung abscess Lung abscesses may also result from infected emboli which arise in other parts of the body and break down into suppuration after becoming lodged in the lung

Pathology The pathological process may be necrotic from the start The area of suppuration breaks down into a small cavity and is surrounded by a zone of edema and exudate in the neighboring alveoli which is not encircled by a definite wall in the acute stage As the suppurative process progresses the area breaks down until the abscess may become one of very large size with a correspondingly marked increase in the collateral zone of exudate Sputum is absent during the formative stage of the abscess and foul expectoration occurs only when communication with a bronchus is affected Usually early in the process pus breaks through into the bronchus and is discharged through the mouth by cough If this type of drainage is insufficient the pathological process continues to extend until a large portion of the lung may be involved On the other hand if drainage is effective the pus is evacuated the area of exudate surrounding the abscess is absorbed and prompt resolution occurs If drainage is only partially adequate the process may become localized a fibrotic wall forms about the area of infiltration and a chronic abscess results

monary embolism pneumothorax or even a pleurisy with effusion One of the outstanding features in the differential diagnosis is that in massive collapse the signs are out of all proportion to the symptoms

Prognosis The patient is not very ill from massive collapse and although he may be short of wind he usually feels quite well He is almost always free from pain but pain is associated with some of the diseases confused with massive collapse

Usually after massive collapse the lung becomes inflated within from two to three days to a week or two Sometimes pneumonia or some other complication sets in

TREATMENT

1 Emergency Treatment The emergency treatment consists in combating shock and collapse

a Force the patient to cough

b One hundred per cent oxygen should be started immediately However some prefer a mixture of five per cent carbon dioxide concentration in oxygen

c For cardiac stimulation 2 or 3 cc of coramine should be given subcutaneously and repeated every four hours

d Recently the bronchoscope has been used to withdraw obstructing substances from the main bronchial tree

e Sometimes moving the patient from side to side in a rocking sort of motion is sufficient to cause the expectoration of the large hemorrhagic gelatinous like mucous mass which is followed by inflation of the lung

2 Prophylactic Measures

a Inhalations of five per cent carbon dioxide and oxygen following anesthesia are of value in the prevention of postoperative atelectasis and should be repeated if there is any evidence of bronchitis

b Encourage deep breathing and frequent changes of position following operation Steam inhalation with tincture of benzoin or menthol to warm and moisten the inflamed mucous membranes is advised

c Excessive use of morphine and hypnotics following operation should be avoided as they tend to restrict coughing and full respiratory movement and favor the retention of mucous in the bronchial tubes

d Avoid tight binders or appliances which hamper breathing

e Guard against upper respiratory infections

LUNG ABSCESS

Lung abscess is a localized suppuration in the parenchyma of the lung and is usually associated with necrosis of pulmonary tissue

sitates variations in therapy In general conservative therapy has proved to be poor during the past 10 years

TREATMENT

1 Preventive Contemplated surgery about the mouth or pharynx including removal of abscessed teeth and infected tonsils should be preceded by a preliminary period during which as much oral sepsis is obtained as is possible Hyperventilation of the lung and coughing should be encouraged after operation as a means of preventing abscess formation

2 Strict bed rest is necessary Fresh air a moderately high caloric diet rich in vitamins and ultraviolet radiation are neces sary accompaniments of bed rest Postural drainage continued for five to six minutes several times a day during which time the in fected lung always occupies the uppermost position is one of the greatest aids in this disease Rest in bed for several weeks after puru lent expectoration has ceased is always indicated

3 In the early stages severe pain and lack of sleep may exhaust the patient and morphine sulfate 0 008 to 0 01 Gm (⅛ to ¼ grain) or codeine sulfate 0 033 Gm (½ grain) administered subcutaneously may be temporarily employed Deodorant inhalations in cases with a distressingly malodorous expectoration have some value

4 A few cases may recover within a period of several weeks with the use of arsenical therapy

5 Chemotherapy has come to occupy a relatively large position in the treatment of acute lung abscess There are on record reports of cases which have recovered through the use of sulfapyridine given in large doses starting with an initial dose of 3 to 4 Gm (45 to 60 grain) followed by 1 Gm (15 grains) every four hours until a suitable blood level has been reached The patient is then placed on a maintenance dose usually 1 Gm (15 grains) three or four times a day to help maintain this level More recently sulfadiazine and sulfathiazole have been used with similarly encouraging results

6 Penicillin has been tried but poor results especially in infants and children have been reported Intramuscular penicillin has been reported to produce improvement but no final cure in lung abscess

7 Bronchoscopy is indicated in order to create a passageway through the swollen mucous membrane of a bronchus it is also

Signs and Symptoms Whenever a patient with pneumonia fails to recover within the usual period of time abscess of the lung must be considered Most cases thought to be unresolved pneumonia are in reality cases of lung abscess The acute onset with a chill sudden rise in temperature and pain in the chest may simulate that of pneumonia Within several days foul pus may be expectorated Fever remains high and the amount of expectoration may be profuse and associated with a distressing paroxysmal cough In extensive cases dyspnea and cyanosis may ensue because of insufficient aeration due to the large amount of pulmonary tissue involved Physical signs are scant in the early stages There is an impaired percussion note and numerous fine moist rales without alteration in the breath sounds Tuberculosis with cavitation may be simulated The right lower lobe is the one most commonly affected because of the relative ease with which the expectorated material reaches it

Diagnosis X ray signs are the most satisfactory diagnostic criteria Early in the disease there is an area of increased density with a rarefied center Later the rarefied center may show the characteristic dense shadow of a shifting fluid level However the area of infiltration may be homogeneous if the cavity is sufficiently large to be detected by x rays or if it is completely filled with exudate Chronic cases of pulmonary abscess may show multiple cavities each with a fluid level The diagnosis should be suspected if the patient expectorates foul pus and runs the clinical course previously described

Chronic abscess in the upper lobe greatly simulates tuberculosis and the differential diagnosis is made by virtue of persistently negative sputum the history onset and course which are usually fairly typical for lung abscess Bronchiectasis has a more difficult differential diagnosis since the two are often associated The diagnosis is made through the use of x rays with lipiodol since in bronchiectasis the bronchiectatic cavities are well outlined by the lipiodol Bronchogenic carcinoma may simulate a lung abscess after it becomes secondarily affected and breaks down Both carcinoma and abscess may be found at autopsy

Prognosis Prognosis is dependent upon such things as the type of abscess and whether the infection is a primary secondary or mechanical one The type of infection alters prognosis and neces

CHAPTER XV

Acute Abdominal Emergencies

The diagnosis of acute abdominal emergencies is of as much importance to the general practitioner and the internist as it is to the surgeon The truth of this statement lies in the fact that the patient with acute pain is usually seen by the general practitioner or diagnostician before the surgeon is called and naturally the diagnosis must be made by the nonsurgical colleagues

When a patient is taken with acute abdominal pain the diagnosis is always difficult because the abdominal distress may be only a manifestation of a disease in some other part of the body unrelated to the abdomen itself For example a patient with pneumonia may have abdominal pain as an early symptom and if an operation is performed on such a patient the fatality rate is quite high yet if this patient with the acute abdominal distress has a peptic ulcer which is perforating or which has perforated a delay in operation might be held responsible for a fatal outcome

There are so many conditions that may cause abdominal pain that an enumeration of them alone would be a lengthy undertaking For practical purposes the diagnosis of the acute abdomen will be taken up in the following manner The law of averages shows that there are five important diseases in men that may be responsible for the so called acute abdominal emergency They are (1) Acute appendicitis (2) acute gallbladder disease with or without stone (3) perforation of a peptic ulcer (4) acute bowel obstruction and (5) acute pancreatitis (Fig 1) In women we must add four more diseases to the list (6) Ruptured ectopic pregnancy (7) acute salpingitis (8) twisted ovarian cyst and (9) rupture of a tuboovarian abscess (Fig 2)

Before commenting upon these disorders it should be emphasized that there are five extraabdominal diseases that commonly cause pain in the abdomen simulating an acute surgical emergency They are (1) Pneumonia (2) coronary disease of the heart (3) lead colic (4) tabes dorsalis with gastric crisis and (5) renal stones These con

necessary to remove a foreign body if this is the agent which started the pathological process

8 Conservative treatment is said to fail in approximately 70 per cent of cases according to various observers and then surgical drainage is indicated Some believe that surgical intervention is the method of choice and should be done as soon as possible after an abscess cavity can be shown to be present Surgeons believe that the opening and draining of a lung abscess is as important as th opening of an abscess in another part of the body Primary lung re section has been found to be the procedure of choice if multiple abscess or extensive destruction in one or more lobes exists if there is secondary bronchiectasis if atelectasis or pneumonitis is unrelieved by bronchoscopic treatment if there is uncontrolled bleeding or if perforation and localized empyema exist

9 Surgical intervention is contraindicated during the acute stage of the disease because it widely disseminates the infective proc ess due to lack of protective barriers Surgery is most satisfactory if instituted after the acute stage is over and before the chronic stage has become well established

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ditions do not embrace all of the diseases that may cause either a genuine or false abdominal emergency but they are the commonest diseases that must be kept first in mind There are innumerable medical conditions that have to be taken into consideration as cirrhosis of the liver acute hepatitis uremia diabetic coma various drug poisonings abscesses of the liver vitamin deficiencies and many other constitutional disorders

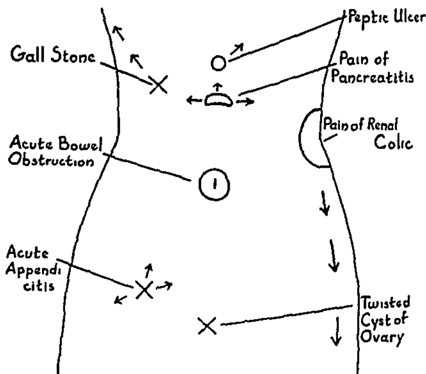


Fig 1—The chief points of pain in various acute abdominal disorders

Diagnosis of Acute Abdominal Pain The importance of making a prompt and precise diagnosis in a case of acute abdominal pain cannot be overemphasized for as stated above an incorrect diagnosis may lead to an operation which is not only needless but which may be detrimental to the patient and even cause his death on the other hand a delay in the presence of an acute abdominal catastrophe may lead to a fatal outcome This kind of diagnosis requires the mustering of a physician s entire diagnostic acumen and the mobilizing of his past experiences and observations on very short notice Such cases

do not permit delay entailed by carrying out elaborate laboratory work. While laboratory studies at times are important for diagnosis of acute abdominal conditions, it must be emphasized that the diagnostic ability of the physician himself with only his God given senses is far more important. Most cases of the acute abdominal type may be diagnosed accurately if the diagnostician takes plenty of time and cross examines the patient skillfully. Many times the diagnosis is

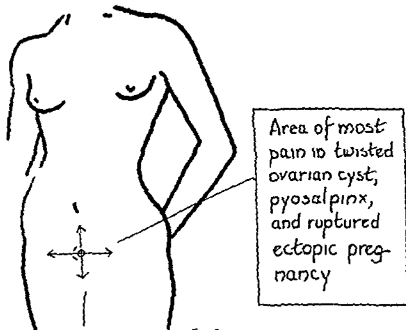


Fig 2

made too swiftly to be precise and one may be greatly embarrassed when the abdomen is opened and it is found that the dramatic snap diagnosis was far from the correct one. By this it is not implied that one should practice waiting and putting off the diagnosis until another day, for such procrastination is also a serious error.

A careful history and painstaking physical examination of the patient are so important that no apologies for extra emphasis are given. The history a patient gives is usually like a textbook description of the disease. The history taking requires more than merely asking the patient about the immediate abdominal disturbance; it includes a careful questioning as to past experiences with abdominal

ACUTE ABDOMINAL EMERGENCIES

	Acute Appendicitis	*Acute Cholecystitis*	*Gall Stone Colic*	*Acute Intestinal Obstruction*	*Perforated Peptic Ulcer*	*Acute Pancreatitis*	*Acute Salpingitis*	*Twisted Ovarian Cyst*	*Ruptured Ectopic Pregnancy*
Age and Sex	Any age Mostly 10 to 40 Either sex	Middle aged Females	Middle aged Females	Any age Either sex	20 to 50 Either sex	40 to 60 Mostly females	15 to 30 Females	18 to 50 Females	16 to 36 Females
Onset	Gradual	Gradual	Abrupt	Sudden	Abrupt	Abrupt	Gradual	Sudden	Abrupt
Nature of pain	At first colicky later localized over area of appendix	Dull merging into colic	Colicky in epigastrium	Cramp-like pains over entire abdomen	Severe pain in upper abdomen	Continuous pain in upper abdomen	Dull aching pain in both lower quadrants	Sharp pain in lower abdomen	Dull pain in back and lower abdomen
Associated Symptoms	Tenderness over right lower quadrant nausea and vomiting	Vomiting and jaundice	Jaundice and vomiting	Vomiting	Vomiting shock	Shock tenderness and rigidity	History of past G C infection	Associated with effort	History of missing periods
Diagnostic features	History of generalized abdominal ache with tenderness and rigidity over right lower quadrant	Tenderness over gall bladder	Women, fair fat around 40 with acute pain in epigastrium and jaundice	Pain vomiting and distention	Pain shock rigidity of abdomen Gurgles gone	Mostly in women who have had gall bladder disturbance	Pain coming on about menstrual time associated with high fever	Lower abdominal pain in women coming on after exercise	Uterine bleeding with enlargement of uterus and subnormal tempera[illegible]

pain and in particular the past history of a similar kind of pain The sequence of events is always of great importance as for example in the diagnosis of acute appendicitis In this disease as has been emphasized down through the years the following events though not always in the same sequence nearly always take place (a) Generalized abdominal pain (b) nausea and vomiting (c) localization of the pain over the right lower quadrant and (d) a rise in temperature

The examination must be painstaking but this does not mean just a careful study of the abdomen alone because diseases of the chest the nervous system and cardiovascular system may be shown to be the cause of the abdominal pain However this fact is uncovered only after elaborate observation of the patient

ACUTE APPENDICITIS

Acute appendicitis heads the list of the acute abdominal emergencies When one considers that it is the commonest surgical condition found in the abdomen the importance of this disease in differential diagnosis is readily seen An early diagnosis and prompt operation are of course primary requisites in the management of this disease Naturally the diagnosis is of greater importance because on it the treatment depends As has been demonstrated time and again a delay in diagnosis often leads to perforation of the appendix with generalized peritonitis which is associated with a high mortality rate Thus the need of an early and careful diagnosis is obvious The operative mortality of acute non complicated non perforated appendicitis is less than one per cent while the mortality rate of all forms of acute appendicitis is about four per cent

If the signs and symptoms of early appendicitis were always of the same kind and intensity the diagnosis would be simple However we know that such is not the case and that many cases of acute appendicitis present atypical features which lead to confusion in diagnosis Most often the difficulty does not lie in the differentiation between acute appendicitis and some other abdominal emergency requiring surgery but between acute appendicitis and a disease of no surgical significance For many years I have been guided by the following axiom when in doubt about the diagnosis of the atypical case —When confronted with a patient who has an acute disease that simulates acute appendicitis and after careful history

and physical examination acute appendicitis cannot be eliminated as the cause then the operation should be done immediately The *opposite stand that is when in doubt wait for further developments* has been in my experience not only an erroneous but a disastrous course to follow An operation performed in doubt that is a legitimate doubt, *will do little harm to the patient even though no* appendicitis is found while failure to operate when appendicitis actually exists may result in perforation and diffuse peritonitis with the subsequent death of the patient

Signs and Symptoms Ordinarily the patient with acute appendicitis is stricken suddenly with a pain over the entire abdomen which soon localizes to the right lower quadrant with most tenderness over the so called McBurney s point We commonly think of the tenderness in acute appendicitis as being localized to McBurney s point but this does not always hold true An inflamed appendix attached to a mobile cecum may give practically no pain upon abdominal palpation but rectal examination will cause the patient to cry out when the tender inflamed mass in the pelvis is touched by the examining finger A retrocecal appendix will show marked tenderness in the right flank with relatively little at McBurney s point and if merely the tip is involved in a gangrenous process the tenderness may be so high *that it simulates gallbladder* disease Occasionally the appendix lies in a position to the left of the midline and we must also bear in mind the possibility of a *situs inversus in left lower quadrant tenderness*

The onset of pain is abrupt and not very severe Usually there is no history of preceding attacks The pain in most cases has the superficial aspect of the good old fashioned belly ache that follows eating green apples In fact most patients after the onset of pain seem to remember something they ate the day before which disagreed with them In days gone by this led to the wrong diagnosis of ptomaine poisoning The patient usually lies on the flat of his back with the right leg drawn up a little to relieve the tenseness and pain Vomiting usually follows the pain and does not precede it The number of *times* the patient vomits is *of some* diagnostic importance for a patient with appendicitis seldom vomits more than a few times With other diseases as gall bladder disease or *gastric crisis* the patient may vomit many many times and lie back

exhausted from the nausea and vomiting The pulse is usually accelerated and there is a slight fever Consideration should be given to the old saying if the fever is above 38 3° C (101° F) look out for something besides appendicitis

Diagnosis The diagnosis of acute appendicitis is usually easy but sometimes it is difficult and occasionally impossible Acute bowel obstruction especially of the small bowel and salpingitis and pelvic cellulitis in women and the gastroenteritis of acute food intoxication are the main diseases of the abdomen which simulate appendicitis Extra abdominal disorders as pneumonia renal and biliary colic lead colic and gastric crisis must be taken into consideration In these puzzling cases not the pain in the abdomen nor the tenderness in the right lower quadrant constitute the diagnostic criteria but the other signs and symptoms which develop along with such pain As for example in acute bowel obstruction there is an abrupt onset of pain colicky in nature with innumerable attacks of vomiting The patient is in greater distress and more on the verge of shock than in acute appendicitis Then too the vomiting may come on before the pain of obstruction sets in A subnormal temperature rather than a fever may be characteristic during the early stages of this disease

In acute salpingitis the associated history of trouble in the abdomen especially of the lower part is characteristic Then again the pain of pelvic cellulitis or salpingitis has a different course than that of appendicitis and the previous history of infection or exposure to infection or of disturbances of the uterus and adnexa is also important in diagnosis The blood sedimentation study may be helpful in acute appendicitis the sedimentation rate is almost normal while it is increased in acute salpingitis

Biliary colic or biliary disease is usually attended by previous spells of pain and tenderness in the right upper quadrant These attacks are often precipitated by the same indiscretions of diet the finding of bile tinged urine or slightly jaundiced sclerae When the urine examination reveals many red blood cells and one is suspicious of renal colic a flat plate of the abdomen should be taken and every attempt made to eliminate renal stone as the causative factor of the colic Gastric crisis and lead and other colics are diagnosed by the presence of other changes

The diagnosis of pneumonia is suspected if the respirations are rapid and if the patient has an anxious expression about the face and a sharp hacking cough If one suspects pneumonia an inquiry should be made about a possible grippal or upper respiratory infection of a day or two before The diagnosis of course is clinched by the physical examination and here percussion is more important than the stethoscope or x rays The earliest and most conclusive evidence of pneumonia is the percussion note which is impaired over the area of consolidation

In children one may frequently see a condition known as acute mesenteric lymphadenitis which is definitely a clinical entity Usually there is a history of a previous sore throat or upper respiratory infection The attack begins with right sided abdominal pain followed by tenderness in the right lower quadrant due to the presence of inflamed mesenteric lymph nodes Nausea and vomiting may be present The fever is higher than in appendicitis in most cases the leukocyte count is not a diagnostic aid because of its variability Experience has taught me that when in doubt as to the diagnosis operation should be done as it is sometimes impossible to differentiate between this condition and appendicitis

ACUTE GALLBLADDER DISEASE WITH OR WITHOUT STONE

Inflammatory lesions of the gallbladder top the list of conditions that produce pain and distress in the right upper quadrant of the abdomen Numerous classifications for the acute diseases of the gallbladder have been suggested but many of them while they are based on physiological and pathological features are too cumbersome or clumsy for clinical application The condition may be said to be characterized by three types of disease (1) Acute catarrhal cholecystitis or hydrops of the gallbladder (2) suppurative cholecystitis and (3) gangrene of the gallbladder

Etiology Gallstones are the most important exciting cause of acute cholecystitis Pyogenic organisms the streptococcus the staphylococcus and the colon bacillus may be the bacterial factors While these organisms, especially streptococci when present in the blood stream may invade the gallbladder without the presence of stones usually gallstones exist

Diagnosis Acute cholecystic disease must be differentiated from duodenal ulcer acute appendicitis renal colic acute pleurisy or pneumonia of the right lower lobe When the clinical signs and symptoms are clear cut the differential diagnosis may be easy but at times difficulty may be encountered The past history history of onset of the present disease and careful physical examination often will be sufficient to clinch a diagnosis When in doubt and when the clinical picture is not complete an x ray examination may disclose a

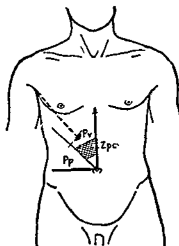


Fig 3—Biliary and pancreatic points of tenderness (Chauffard) Pv gall bladder point Pp Desjardins s pancreatic point Zpc pancreatico choledochian area

stone in the kidney ureter or the gallbladder itself An x ray examination of the chest may cause one to shift from an impression of cholecystic disease to inflammatory condition of the lung involving the right leaf of the diaphragm Great caution must always be exercised in analyzing the case so that an acute appendicitis will not be overlooked and pass untreated into a stage where even an operation may fail to save the patient s life

Acute Catarrh or Hydrops of the Gallbladder

The acute catarrhal cholecystitis may or may not be associated with stone However stones occur in about 90 per cent of cases There may be varying degrees of edema of the gallbladder wall and by the same token there may be evidences of mild moderate or severe inflammation

Signs and Symptoms In acute cholecystitis of the catarrhal type the individual is often taken suddenly with pain in the right upper quadrant chills and fever When a gallstone is present the pain may be more colicky in type and the symptoms more severe As a rule acute cholecystitis of the inflammatory type occurs in individuals past the age of 40 years It is three times as common in women as in men Tenderness over the area of the gallbladder is found in all cases The gallbladder is distended and palpable in about one fourth of the cases Chills or chilly sensations occur in practically all cases and jaundice in approximately one third of them When stone is present the symptoms and signs are more prominent and the course of the disease is longer Without stone the acute hydrops of the gallbladder lasts from four to eight days if stone is present it continues for one to two weeks The pain and tenderness over the right upper quadrant is the most characteristic feature of the disease The pain may be referred into the back or up under the right shoulder The temperature usually reaches its acme on the first day rising to 39 5° or 40° C (103 or 104 F) Vomiting is present in about three fourths of the cases This disease may be confused with acute appendicitis especially when the pain of appendicitis is referred upward to the right upper quadrant

Course and Prognosis The outlook is favorable in this kind of cholecystitis Most patients resolve promptly within a week unless such complications as suppuration or gangrene set in If stone is present the chances of a recurrent attack must always be kept in mind

TREATMENT

Within recent years the tendency in the treatment of cholecystitis has been to be more radical than formerly While it must be admitted that acute cholecystitis does not present the surgical emergency of acute appendicitis sometimes an operation must be performed to save the patient from suppurative cholecystitis and peritonitis or from perforation of the gallbladder However most cases respond favorably to palliative treatment as

1 Large hot stupes to the abdomen

2 Sedatives as small doses of codeine sulfate 0 033 Gm (½ grain) pantopon 0 011 Gm (⅙ grain) or morphine sulfate 0 018

Gm (1/4 grain) given hypodermically for the relief of pain and spasm

3 Duodenal drainage advocated by many observers and proved to be effective in many cases

4 Intravenous solutions as 1000 cc of ten per cent glucose in normal saline solution every day

5 Atropine 0 0003 Gm (1/00 grain) hypodermically or pheno barbital 0 033 Gm (1/ grain) orally three times daily

6 Surgical treatment should be considered when the fever chills pain and enlargement of the gallbladder persist for three days or more If stone is present then surgical treatment is without doubt the procedure of first choice

Suppurative Cholecystitis

The difference between acute cholecystitis of the catarrhal form and acute suppurative cholecystitis is more of degree than of kind for the acute catarrhal type may progress and become a suppurative form The pathological changes in the gallbladder are more severe in the suppurative type and necrotic lesions occur in the mucosa of the gallbladder The extensive infiltration of the gallbladder wall may lead to vascular changes which if severe enough develop into areas of infarction with gangrene and perforation

The tenderness and pain in this form may not be any greater than in the simple catarrhal cholecystitis and it must be remembered that these symptoms are not exact measuring sticks of the degree of inflammation present in the gallbladder More reliance may be placed upon the higher fever more severe and frequent chills and greater rise in leukocytes with a high percentage of stab forms in the differential count When these evidences of severe infection last for a few days the tendency is to give up waiting and depending upon medical or palliative measures and to operate at an early date The mortality rate in the acute suppurative type increases if surgery is *delayed more than five days Statistics on the mortality* rate of patients not operated upon show that the average rate ranges from 10 to 20 per cent

Gangrene of the Gallbladder

Gangrene and perforation or abscess of the gallbladder are com plications that occur when a cholecystitis fails to heal and becomes

progressive By far the greatest number of gallbladder perforations occur in cases where nature already has built up a cofferdam about the inflamed viscus by means of the omentum and hence perforation results in the formation of a localized abscess corresponding to that seen in appendicitis If perforation takes place without walling off by the omentum the picture is one of sudden onset of generalized abdominal pain with widespread rigidity and it is often confused with the acute perforation of a peptic ulcer

It is said that a ruptured gallbladder is found at autopsy or operation in about 12 per cent of these cases While there is a great difference in reports and opinions concerning the incidence of perforation and pericolic abscess there is no doubt that in general the mortality rate is very high if palliative measures are used persistently However one s judgment in the management of these cases must be tempered a good deal by his own experience and immediate observations If the cholecystitis appears to be mild early operation may be postponed On the other hand when the diagnosis is clear-cut and the general condition of the patient is growing worse with the signs and symptoms indicating a severe inflammatory lesion early operation seems safe and attended with a lower mortality than late surgery Those who wait for the acute gallbladder to cool off must be ready to shoulder the responsibility of a mortality rate that runs from 15 to 20 per cent while those who operate before the fourth day of the disease assume responsibility of a five per cent mortality rate In general it may be stated that mild cases may be treated palliatively and severe cases treated more radically and surgically

Gallstone Colic

Gallstones form in the gallbladder and occasionally in the larger ducts of the biliary tract They occur more frequently in women than in men probably due to the difference in cholesterol metabolism in men and women Gallstones may be divided according to kind into (1) The pure cholesterol stone (2) the one composed of cholesterol and bile pigment and (3) another made up of cholesterol bile pigment and salts of magnesium and calcium Cholesterol stones are usually single the other kinds are multiple In the multiple type there may be several or several hundred stones

Since at this time it is gallstone colic that is being discussed the

diagnosis of gallstones will be discussed briefly It must be remembered that gallstones may lie in the gallbladder symptomless for a long time On the other hand, gastric disturbances as belching indefinite pain in the abdomen and abhorrence for certain kinds of food especially fatty may be present for many years before the true nature of the disease is exposed Cholecystography is usually very effective in diagnosing gallstones

Signs and Symptoms 1 Pain usually comes on abruptly and is excruciating in type It commences in the epigastric area in most cases and radiates over the entire upper abdomen into the right chest It is paroxysmal in type and frequently becomes more severe as time goes on

2 There is sweating at times chills the pulse is weak and the patient is on the verge of collapse

3 The patient nearly always vomits not once but several times

4 Jaundice occurs but only after several hours as a rule Sometimes *several days elapse before jaundice begins*

5 After the succession of attacks the pain may stop as abruptly as it began and never return again This happens when the stone slips out of the duct into the ampulla or the intestine The stone may plug the cystic duct and cause hydrops of the gallbladder In this case there is no jaundice but the gallbladder is tender and distended Sometimes the stone becomes impacted in the common duct resulting in a long continued and occasionally permanent jaundice A stone may produce partial obstruction and lead to suppuration in the biliary tree In these cases jaundice fever chills and paroxysms of pain come and go over a period of years unless the obstruction is relieved by operation

TREATMENT

1 The patient usually lies in a fixed cramped position and takes exception to being examined

2 Pain must be relieved at once by giving morphine sulfate 0 016 Gm (¼ grain) with atropine sulfate 0 0008 Gm (1/75 grain) hypodermically This must be repeated every two or three hours

3 Sometimes an intravenous injection of calcium chloride 10 cc of a five per cent solution eases the pain This injection must be given slowly at the rate of 2 cc per minute for if given more rapidly severe nausea and vomiting usually occur

4 A hot wet fomentation placed over the entire abdomen often gives considerable comfort

5 If the patient is not vomiting too much, a tablet or capsule containing atropine 0 0006 Gm (1/100 grain), and phenobarbital 0 1 Gm (1½ grains) given orally may serve to alleviate the distress

PERFORATION OF A PEPTIC ULCER

Peptic ulcers may be gastric or duodenal and either acute or *chronic* *While the preceding clinical features may vary a good deal* depending upon the location position and size of the peptic ulcer the event of most importance is the acute perforation which may occur *in any* type of ulcer There are few conditions in which the prompt recognition of this emergency is of greater importance since the patient s condition and chances for recovery become worse with every *hour s delay* Therefore it is of little or no consequence to be able to identify beforehand the exact location and kind of lesion causing the perforation, for while it is always desirable to make as exact a diagnosis as possible it is *imperative to recognize* the fact that a perforation has occurred and that an immediate operation is necessary

Etiology Certain contributory factors may be mentioned as causes for perforation of a peptic ulcer Excessive physical activity direct trauma to the abdomen and sudden physical effort have been included However perforation may occur in the absence of any of the so called exciting causes

Signs and Symptoms Perforation of a peptic ulcer may occur at almost any age and at any time It may take place when the stomach is empty but is more likely to occur when the stomach is filled with *food or liquids or both* and the drinking of a large quantity of cold beer preceding the rupture of an ulcer is not at all uncommon The patient attributes his pain to the cold beer but careful history and examination will generally reveal the true story

Duodenal ulcers are approximately four times as common as gastric ulcers and perforated ulcers bear about the same ratio Usually perforation is preceded by a history of recurrent attacks of ulcer but this is not always the case Perforation may occur in an individual who has never had any symptoms referable to the ulcer or the patient may be an alcoholic who denies any previous stomach distress He has

had it but pays little heed to it thinking that it is due to his use of liquor of uncertain quality Males are much more prone to ruptured ulcers than females the proportion being about 25 or 30 to 1

The symptoms that develop when perforation actually occurs are very definite and need little description The symptoms may be divided into three stages (1) There is an abrupt onset of violent pain in the upper abdomen Usually this pain quickly spreads over the entire abdomen down into the pelvis and both flanks but at times it is limited to the right side with tenderness in the lower right quadrant as its chief sign This is due to gravitation of the escaped stomach contents down the gutter formed by the ascending colon and the lateral abdominal wall and the diagnosis of appendicitis is a natural mistake Vomiting often occurs along with the pain bright red blood may be seen in the vomitus and it is well to remember that every now and then a perforating ulcer bleeds Conservative treatment in such a case might result in a fatality The presence of generalized peritoneal irritation in the perforated ulcer should differentiate it from the pure case of bleeding ulcer Sometimes the pain is so severe that the patient collapses and lies perfectly quiet because any effort to move exaggerates the pain In this initial stage the pulse becomes rapid weak and thready and the blood pressure falls to well below normal The patient is pale and cold and is often covered with a clammy sweat Palpation at this time usually reveals rigidity of the entire abdominal wall Although the abdomen is generally tender there is usually a point of greatest tenderness over the epigastric area This tender area and the spread of the pain downward toward the pelvis are factors that may be helpful in differentiating the condition from some catastrophe that occurs above the diaphragm but simulates the acute abdomen

(2) Within one half to two and one half hours after the initial shock a reaction sets in This is characterized by great improvement in the patient s condition Color comes to his face the pulse becomes slower and of better volume The pain diminishes and vomiting ceases In this stage the diagnosis may be more confusing than at any other period of the emergency *Improvement may develop in all directions but there is one outstanding sign of perforation which occurs at the very beginning and persists throughout—that is rigidity of the abdominal wall* This rigidity is due to the irritation of the

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peritoneum by the escaped acid stomach contents which at first cause a chemical peritonitis the amount of rigidity is an index of the amount of irritation below the peritoneum The liver dullness is obscured by the presence of air in the abdominal cavity but this sign is not of much diagnostic value

(3) If the patient is not operated the third period develops within 24 hours This is the period of generalized peritonitis In this stage the temperature is no longer subnormal but begins to rise The heart becomes rapid and weaker Symptoms of dehydration usually set in and if these are not combated by administration of fluids the typical Hippocratic facies develops The patient in this stage appears very ill and the presence of a generalized peritonitis hardly ever escapes the clinical observer

Throughout all stages it must be emphasized again that the chief identification mark of a perforation of a peptic ulcer is the rigidity of the abdominal wall which at first is associated with retraction and later with distention of the abdomen but the tenderness and rigidity continue unabated

Diagnosis The differentiation of nonsurgical conditions as pneumonia the colics gastric crisis and other medical diseases may cause considerable difficulty at times The awful consequences that may develop from neglecting to operate upon the acute perforation of a peptic ulcer are such that the recognition of this condition constitutes one of the greatest responsibilities that confronts a practicing physician Gallstone colic renal stone acute appendicitis and gastric crisis seldom present any great difficulty in differential diagnosis

If one keeps in mind that a perforation of a peptic ulcer is characterized by abrupt onset of intense abdominal pain associated with absolute rigidity of the abdominal wall and a point of localized tenderness in the ulcer bearing area I believe the correct diagnosis will usually be made Acute hemorrhagic pancreatitis or acute mesenteric thrombosis may each cause a violent pain in the abdomen followed by prostration yet the abdominal rigidity is not as constant and universal as in perforation It is well to bear in mind that at times one is confronted with referred pain due to medical conditions above the diaphragm which simulates that of perforated ulcer Therefore every patient should be studied carefully for evidences of pneumonia or an acute heart condition before a final diagnosis of perforation is

made Whenever there is a definite question concerning the presence or absence of perforation an x ray examination of the abdomen for free abdominal air should be conducted Free air in the upper abdominal region is found in about one half of the cases of perforated ulcer The visualization of free air under the diaphragm by an x ray film is positive proof of a ruptured viscus but a negative picture does not mean that perforation is not present A positive x ray picture is often a valuable aid when perforation has occurred 24 hours or more previously and the diagnosis is doubtful

Prognosis If operation is performed in cases of acute perforation before 12 to 16 hours have elapsed most of them will recover with a remarkably easy convalescence If the patient is old or suffering from one or a combination of degenerative diseases the prognosis is not so good In general the mortality rate in acute perforation of an ulcer is 25 per cent but the younger stronger patients will almost all recover if operated in time

TREATMENT

The treatment is of course entirely surgical but a few measures have to be carried out in the period that elapses between the acute perforation and the arrival of the surgeon in the operating room

1 The patient should be given 0 02 Gm (⅓ grain) pantopon or 0 016 Gm (¼ grain) morphine with 0 0008 Gm (1/ grain) atropine hypodermically at once to relieve the pain

2 Further collapse may be combated by administering 2 to 5 cc of adrenal cortex substance intramuscularly

3 Intravenous solutions may be given while preparations are being made for the operation 1000 cc of ten per cent glucose in saline may act as a bulwark to the circulatory system or 300 cc of blood plasma may be administered immediately as a preoperative measure

4 Time should not be lost by going through unnecessary maneuvers the main thing is to bring the patient to the operating room as quickly as possible and to have the operation done promptly

ACUTE INTESTINAL OBSTRUCTION

The following discussion is not given with the thought that there is a medical aspect to the treatment of acute intestinal obstruction

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more severe than other symptoms The abdomen is usually distended unless the stricture is high in the jejunal area Auscultation over the abdomen may reveal high pitched tinkling peristaltic sounds which are suggestive of obstruction Excessive vomiting leads to dehydra tion and alkalosis The sodium chloride of the blood falls and the nonprotein nitrogen creatinine and potassium rise The obstruction of the flow of the bowel contents is not as important as the damage to the intestinal wall The reason for some patients developing early shock and collapse in bowel obstruction while others do not cannot be explained by the kind of lesion present one type of intestinal involvement may produce mild symptoms and signs in some individ uals and a severe grade in others Frequently patients become toxic within a few hours when there is a constriction of the jejunum The pulse becomes rapid the pain more marked vomiting severe and the patient is very restless pale cold and clammy

Diagnosis The differential diagnosis of obstruction of the small bowel as stated above is often difficult however lack of early and proper diagnosis usually cannot be attributed to inadequate knowl edge of the condition but to lack of thoughtfulness concerning the possibility of the presence of this condition The abrupt onset of pain and vomiting without any other apparent cause should always make one think of acute bowel obstruction When there is an old operative incision scar upon the abdominal wall this should further suggest the presence of an obstructive lesion Acute appendicitis acute gallbladder disease perforation of a peptic ulcer acute pancre atitis and pelvic diseases in women must all be considered in the differential diagnosis Mesenteric thrombosis or embolism is rare but simulates obstruction very closely Other evidence particularly conditions that may lead to thrombosis or embolism as advanced age portal obstruction or irregular heart must be taken into considera tion

Acute intestinal obstruction presents certain characteristic fea tures which may be given as follows

1 After careful history has been taken palpation of the abdomen may reveal a generalized distention with moderate rigidity On aus cultation of the abdomen intestinal gurgles are found to be greatly increased and the rushing of these intestinal sounds gives one the

but on the grounds of diagnosis and management preliminary to surgery Patients with acute intestinal obstruction are frequently seen first by the practitioner and diagnostician and later by the surgeon

When a patient is seized with colicky pain associated with vomiting bowel obstruction must always be kept in mind Of all the conditions responsible for the acute abdominal emergencies bowel obstruction is most often misdiagnosed Furthermore it is the one acute abdominal emergency in which early diagnosis and prompt surgery are associated with favorable results while delay is apt to end disastrously for the patient In this emergency hours count more than in almost any other except the perforations There was an old axiom in surgery which is as true today as when it was originated that is never to let the sun go down on a case of acute intestinal obstruction In those days as well as now it was well known that early operation meant early recovery while late operation meant retarded or no recovery

Etiology Many classifications of bowel obstruction have been proposed The simplest and most usable one is the following

1 Bowel obstruction in infancy and early life due to intussusception and volvulus

2 The acute obstruction of middle life usually involving the small bowel and caused by strangulation of a hernia or obstruction due to old adhesive bands in the abdomen

3 The bowel obstruction of advanced years usually found in the large intestine and caused by carcinoma

Signs and Symptoms The symptoms and clinical course of acute obstruction of the small bowel vary according to the site of the stricture In general pain vomiting and distention of the abdomen are the main features Tenderness may be present but is not necessarily localized in any particular area As a rule there is no rigidity except during the peristaltic rushes After a varying period of a few to 24 hours depending upon the degree of obstruction and disorder of blood supply to the intestinal wall constitutional symptoms may occur They include rapid pulse a falling blood pressure and evidence of oncoming peripheral vascular collapse and shock

Pain is the most important feature of all because it is always present Nausea and vomiting almost always occur and may be much

TREATMENT

1 The treatment of acute intestinal obstruction is frequently surgical but it must be emphasized that the fluid balance should be maintained by the administration of 2000 cc of ten per cent glucose in physiological saline solution intravenously every 12 hours A trans fusion may be necessary The patient should receive nothing by mouth

2 The lower segments of the small bowel may be unloaded by the use of the Miller Abbott tube The patient is sent to the x ray department for passing the tube through the stomach into the bowel

3 When strangulation of the bowel is present operation should be performed within the first few hours after entrance to the hos pital In the presence of obstruction without diagnosis of strangula tion drainage is instituted If this is unsuccessful in 12 hours and the patient is in good condition immediate operation is advised

4 The administration of morphine or pantopon is rarely advisa ble The masking of the symptoms following their use may lead the patient or even the physician and especially the patient s relatives into believing the patient s disease has begun to clear up without operation

Volvulus

Volvulus is strangulation of the intestine due to twists kinks or knots It is caused by twisting of the intestine upon its mesenteric axis resulting in occlusion of the lumen Congenital irregularities in the length of the mesentery or of the intestine or an acquired redun dancy of the tube promoted by constipation may be factors Trauma as a consequence of falls jumps or any physical shock as well as any agent that induces overactive peristalsis may produce volvulus The weight of a fecal mass or tumor pressure from outside the intestine rough manipulation of tissue during laparotomy or paresis of the intestine following surgery are all reported to be responsible at one time or another

Volvulus is seen most frequently in males past middle age In half the cases the sigmoid flexure is involved The ileocecal region is the next commonest site for this malady The small intestine is involved in a lesser number of cases

Signs and Symptoms The symptoms and findings are those of acute intestinal obstruction Colicky pain is at first restricted to the

impression that the bowel is making a violent effort to overcome some obstruction In the earlier periods these intestinal noises may be continuous and violent Later on, the bowel seems to tire out and there are periods of quiescence in which no sounds are heard alternating with periods of rushing activity Attention to the stethoscopic examination of the abdomen in these cases is of great diagnostic importance One must not be thrown off the diagnostic path by the presence of fluid in the abdomen accumulated as the result of peritoneal irritation since it may alter the auscultatory findings

2 Chemical examination of the blood is apt to show an early disturbance of the electrolyte balance and a rise in nonprotein nitrogen Alkalosis low blood chlorides, and a high nonprotein nitrogen occur if the obstruction is high in the small bowel

3 An x ray examination may be helpful in that the stepladder type of pattern caused by distention of the small bowel above the obstruction is an important diagnostic aid X ray examination should be made after the fluid has been removed from the stomach and before an enema is given If there is a question of differential diagnosis between large and small bowel obstruction the truth is usually obtained by injecting a small amount of barium per rectum If there is any doubt x ray examination should be repeated in four or five hours Some say a barium enema is not wise while others advocate its use

Chronic bowel obstruction is usually of the large bowel and is caused by carcinoma However acute manifestations may come on suddenly because a partial obstruction due to growth may have added to it an inflammatory lesion which causes a sudden swelling of the obstructing mass and practically complete obstruction of the large bowel ensues In these cases the patient usually is an older individual and difficulty with the bowels precedes the acute manifestations Pain is usually not so severe in large bowel obstruction as in the small bowel type but distention is much greater The distention may be acute and sudden or it may be insidious and of mild grade When a question of large bowel obstruction arises a barium enema may be given in order to localize the point of the obstructing lesion The site of the obstruction may be found at times by simple rectal examination but more often it is higher in the sigmoid or descending portion of the large bowel Surgery is called for in these cases

TREATMENT

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Signs and Symptoms The symptoms and findings are those of acute intestinal obstruction Colicky pain is at first restricted to the

site of the obstruction but rapidly spreads over the abdomen Sudden cessation of pain with continuance of other symptoms is of serious import Vomiting begins soon after the onset of pain it is at first entirely reflex but after a few hours becomes stercoraceous Abdominal distention is often marked When the obstruction is high in the tube the distention is confined to the upper abdomen until late in the course of the disease Shock of various degrees is frequently noticeable in patients with acute intestinal obstruction Dehydration results in part from the continued vomiting and sweating but probably also from a disturbance of the acid base regulating mechanism leading to a reduction in the sodium chloride content of the blood The urine is usually scanty and commonly contains albumin Nitrogen retention may be found in the blood The leukocyte count generally rises during high obstruction and when the intestine or its mesentery is damaged The bowels usually do not move spontaneously in an acute attack although the material in the tube distal to the obstruction may be discharged in one or two spontaneous movements If the obstruction is incomplete diarrhea may occur Blood may be passed after strangulation and peristaltic movements may be visible on the abdominal wall Hyperactive peristaltic sounds are heard characteristically although they are not invariably present

X rays of the abdomen reveal a distended bowel often with step ladder formation The common clinical picture of congenital volvulus is one of acute obstruction of the second or third portion of the duodenum with bilious vomiting constipation and rapid wasting

Prognosis Twists kinks and knots have been cured spontaneously or by postural treatment and massage but when the obstruction has been sufficiently acute to cause shock and stercoraceous vomiting it is doubtful that the patient can recover without surgical treatment The hope of ultimate cure by surgery diminishes with each hour of delay Untreated acute obstruction may lead to death within a few hours to ten days

TREATMENT

The usual treatment of acute obstruction due to volvulus is surgery Attempts to relieve vomiting and abdominal distention should be instituted by repeated enemata and Wangensteen suction At times the latter measures accomplish release of the obstruction Dehydration should be combated by parenteral fluids Sedation should be

administered judiciously and rarely before the diagnosis is definitely made

Intussusception

Intussusception is the invagination of one portion of the intestine into another It is seen with the greatest frequency in infancy and is at this age the commonest cause of acute intestinal obstruction Usually the upper part of the intestine is invaginated into the lower but the reverse may occur Invagination may take place high in the intestinal tract The so called intussusception of the dying is frequently encountered in autopsies made upon infants it usually involves but a few inches of the intestine and is probably produced by the death agony

Etiology Intussusception appears twice as often in males The cause for the phenomenon is obscure In most cases it occurs in children who have apparently been in perfect health

Pathology Animal experiments have shown that intussusception is caused by irregular action of the muscular walls of the intestine As invagination takes place the mesentery is drawn in with the bowel to allow intussusception to occur the mesentery must be unduly stretched long or lacerated Invagination does not necessarily produce either obstruction or strangulation but both are generally present and are the reason for the symptoms Traction upon the mesentery leads to obstruction of its vessels with consequent congestion edema hemorrhage and even gangrene Obstruction is chiefly due to swelling but may be due to dragging of the mesentery which brings the apex of the tumor against the side of the bowel or bends the intussusception The invagination as a rule includes all the coats of the intestine Failure to reduce the intussusception within the first two or three days is due to swelling from edema Adhesions too may prevent reduction but usually only after several days Gangrene and consequent sloughing occur much more often in acute than in chronic cases Portions of intestine may then be passed In chronic cases shreds of intestine may be discharged for several weeks

Signs and Symptoms The patient is taken suddenly ill with severe abdominal pain and vomiting The pain is paroxysmal recurring every few minutes The vomiting is first of the contents of the stomach later of bile and is often projectile The abdomen is relaxed and a mass can generally be felt in the epigastrium, in the

left *iliac fossa* or by rectum In some cases the mass protrudes from the anus The description of this mass as sausage shaped is accurate when the invagination is large During manipulation or during an attack of pain the tumor may become more prominent By rectal examination the palpable mass resembles the os uteri The examining finger is usually covered with bloody mucus whether or not a tumor is palpable When the tumor protrudes it is usually a deep purplish color and may be gangrenous It has been mistaken for prolapse of the anus polyp and even hemorrhoids

There may be one or two loose fecal stools after which only blood or blood and mucus are passed Restlessness is followed by prostration and even collapse with pallor flaccidity cold extremities feeble pulse and at times a subnormal temperature Tenesmus is common if the tumor is rectal in location In some cases there is absence of peristaltic sounds

In acute cases the condition grows rapidly worse The vomiting and pain continue and after the second or third day the abdomen becomes tympanitic Dehydration appears quickly There is a steady increase in prostration and toward the end a rapidly rising temperature which may reach 41 1 C (106° F) before death occurs If the symptoms continue longer the findings of peritonitis are superimposed

In chronic intussusception the onset and the manifestations are less dramatic The obstruction of the lumen is incomplete and the changes in the bowel itself are less pronounced This type begins with vague intestinal symptoms Pain vomiting and melena are often absent Progressive loss of weight constipation or diarrhea is seen Only the presence of the tumor leads to recognition of the morbid state

Prognosis Spontaneous reduction of intussusception is known It is possible that some cases of severe colic are really cases of mild intussusception which undergo spontaneous reduction Intussusception may be cured spontaneously by sloughing of the invagination and preservation of the continuity of the intestine by adhesions but such fortunate events are not to be expected The mortality in untreated cases is close to 100 per cent while in cases operated on within 24 hours it is no more than 10 per cent The prognosis depends more upon early treatment than upon the age of the patient

of the degree of intussusception Late cases are liable to exhibit pronounced toxemia and shock Delay is less serious in the case of incomplete obstruction but even these should be subjected to surgery at the earliest possible moment Recurrence of the condition is rare

TREATMENT

Laparotomy should be performed without delay when the diagnosis of acute intussusception is made Traction under anesthesia has brought about reduction without operation but this procedure is not likely to be successful in unskilled hands When gangrene or an irreducible mass is present the involved segment must be resected

The fluid balance of the patient must be maintained The quantity of blood lost in the stools is not as a rule great enough to require transfusion Violent cathartics should be avoided in the postoperative period

CHAPTER XVI

Acute Abdominal Emergencies

(Continued)

ACUTE PANCREATITIS

Although acute pancreatitis is not a common abdominal catastrophe it constitutes one of the most difficult and serious diagnostic problems in medicine and surgery and has one of the highest mortality rates of all acute abdominal emergencies It is an inflammation of the pancreatic tissues due to infection The term acute pancreatitis is one that formerly implied a very serious and usually fatal condition The terms acute hemorrhagic and acute necrotic pancreatitis were looked upon as synonymous with acute pancreatitis More recently acute pancreatitis has been differentiated into the simple or so called interstitial or edematous type and the necrotic or hemorrhagic form Obviously the simple or non necrotic type is one associated with symptoms and signs that are much milder and more benign than those found in the hemorrhagic form It must be kept in mind that the difference in the lesion of these two types is a matter of degree only and not of fundamental pathological findings

Etiology The cause of acute pancreatitis is closely bound up with gallbladder disease The most generally held view is that the ampulla of Vater becomes occluded and a flow of bile travels from the common duct into Wirsung s duct of the pancreas The irritation to the setup in the pancreas may be mild or severe and the subsequent symptoms and signs are thereby determined A gallstone or even edema of the ampulla of Vater may be sufficient to cause pancreatitis in certain cases depending upon the anatomical relationship of the pancreatic and common bile ducts Investigators have challenged this commonly held explanation of the bile flow into the pancreas as a chief cause While the argument cannot be settled it is true that most cases of acute pancreatitis are associated with gallstones gallbladder disease infectious process or some disease of the ampulla of Vater In many cases there is a history of recent infection pancreatic

injury alcoholism overeating or disease of the abdomen Obviously the patient is usually in the upper age group because the disease is commonly associated with gallbladder trouble Furthermore the patient is usually a stout female

Signs and Symptoms As acute pancreatitis may be of the mild benign or the severe hemorrhagic forms it must be emphasized that the mild type may develop into the more severe one within a period of a few hours The signs and symptoms that occur in the fulminating acute form will be discussed here

The clinical signs and symptoms of acute hemorrhagic pancreatitis are fairly distinctive and while they may suggest other acute abdominal emergencies there are a few features which serve to differentiate this disease from others that simulate it The onset is usually abrupt and is characterized by severe agonizing pain across the upper portion of the abdomen which may radiate to the back and shoulders Vomiting usually develops and the abdomen becomes distended rather early in the course of the disease The pulse grows rapid and weak and the patient is pale and appears to be on the verge of collapse Sometimes actual peripheral vascular collapse or shock develops As a rule there is no moderation in the degree of the pain it is intense from the start and continues to be so While the clinical features may vary a good deal severe pain abdominal rigidity pallor or cyanosis and a clamminess of the skin are practically always present The temperature may be subnormal or slightly elevated and the leukocyte count is usually 10 000 or more

From this description one can readily see that many other acute abdominal emergencies may produce a similar picture and consequently the differential diagnosis is very difficult To suspect the presence of this disease is one half of the diagnosis Within recent years several laboratory tests have been devised which are helpful in diagnosis Particular attention is directed to the tests of pancreatic ferments in the blood and urine The most popular ones are the serum amylase and the serum lipase tests While the serum amylase is probably not as precise as the lipase it seems to be of greater clinical value because its determination requires only one hour and the lipase test takes 24 hours to perform

Serum Amylase Test The principle of this test is that the serum containing the amylase is allowed to act on a substrate of a starch

suspension which it breaks down into sugar The amount of sugar produced in 30 minutes incubation indicates the quantity of amylase present in the serum Normally this amounts to about 20 mg per cent and is increased in acute pancreatitis and secreting pancreatic adenomas

Serum Lipase Test Lipase in the serum hydrolyzes the neutral fat olive oil breaking it down into glycerol and fatty acid The fatty acid is determined by titration with sodium hydroxide Comparison of the 24 hour incubated specimen with an inactivated control gives the result in cubic centimeters of twentieth normal sodium hydroxide The average range in this test is 0 5 to 1 0 cc up to 1 5 cc which is the high normal The increase in serum lipase occurs in the same conditions as increased amylase

TREATMENT

The treatment of acute pancreatitis is at its best quite unsatisfactory What is accomplished by surgery in these cases is rather circumscribed Surgical treatment offers little more than strictly medical treatment however one advantage in favor of the surgical approach is that if perforation of a viscus or some other abdominal catastrophe is present it may be dealt with satisfactorily In this acute abdominal emergency as in others if any uncertainty in the diagnosis arises an abdominal operation must be done so a condition is not overlooked that may be benefited by surgery

1 Stop all intake by mouth and administer fluid by rectum

2 Morphine 0 016 Gm (¼ grain) and atropine 0 0006 Gm (1/100 grain) may be given frequently enough to control the pain

3 Peripheral vascular collapse may threaten the patient s life Therefore 1000 cc of ten per cent glucose in saline should be given rather rapidly intravenously at once

4 If blood plasma is available 300 cc should be given as soon as possible

5 Adrenal cortical substance 5 cc intramuscularly may be repeated several times at two-hour intervals

6 Large hot wet turpentine stupes on the abdomen are warranted not only because of the value of heat but also because they immobilize the abdomen and tend to ease the abdominal pain

MESENTERIC THROMBOSIS

When a patient develops acute abdominal pain the common disorders should be considered first These are appendicitis gallstones pancreatitis bowel obstruction and perforation of a peptic ulcer In women three additional disorders acute salpingitis ruptured ectopic pregnancy and twisted ovarian cyst must also be kept in mind There are however other conditions which less frequently produce acute abdominal catastrophes Among these is occlusion of the mesenteric vessels caused by thrombosis and embolism It is often considered a fatal disease though this is not always true because there are mild grades of mesenteric thrombosis which invariably heal While the mortality rate is placed at approximately 92 per cent this is too high except for those cases which are characterized by the plugging of the large branch of a mesenteric vessel

Etiology The causes of mesenteric thrombosis may be given as follows

1 Arterial occlusion
   a An embolus from a cardiac vegetation
   b From an atheromatous plaque
   c From a mural thrombus in one of the cardiac chambers
2 Venous type
   a An injury to the abdominal vessels
   b A ligation or a crushing of the veins at operation
   c Strangulated hernia
   d Extension from the portal veins or even from the splenic veins

As far as diagnosis and treatment are concerned it does not make much difference if the disease is one of the arterial or venous system

A mesenteric embolus usually follows a thrombus which originates in the left side of the heart or in an arteriosclerotic aorta A mesenteric artery may also become thrombosed due to arteriosclerosis leading to narrowing and followed by sluggishness of the circulation and finally thrombosis The veins of the mesenteric system may become plugged because of disease of the veins themselves suppurative conditions within the abdominal sac strangulation of hernias and occasionally trauma Larson in a study of 36 cases of mesenteric vascular occlusion in which autopsies were performed found that a mural cardiac thrombosis was the commonest cause of embolism of the mesenteric artery Arteritis and arteriosclerosis most

frequently produced thrombosis venous occlusion most often resulted from septic processes in the gastrointestinal tract pelvis or lower abdomen

Signs and Symptoms The clinical picture of acute mesenteric thrombosis as it is described in textbooks gives the impression that the average case sets in abruptly with great pain and profound shock and that death follows within a few days This may occur but the usual clinical case in my experience has not followed this pattern Before discussing the clinical features of mesenteric thrombosis I should like to emphasize the fact that they depend to a large extent on the completeness of the occlusion the suddenness of its development and the degree of anastomotic circulation When the occlusion is sudden the onset of pain is abrupt followed by inadequate blood supply infarction occurs and is identified clinically by the presence of blood in the vomitus Blood may also be found in the stool, but this is a later manifestation coming on 24 to 48 hours after onset In sudden occlusions the shock may be so great that death occurs within a few hours

More commonly however the disease starts with moderate pain and shock and little or no blood in the stool In this milder type, the only symptoms during the first 24 to 48 hours may be colicky abdominal pain nausea and vomiting tenderness in the abdomen fever and rapid pulse rate these are not positive identification marks of any particular disease Sometimes the abdominal distention pain and rigidity and slight fever are mistaken for evidences of incomplete bowel obstruction After the first 36 to 48 hours the pain becomes steadier the shock more marked the abdominal tenderness more severe and the temperature and pulse rate higher One is led to believe that the patient has an unexplained form of peritonitis It is true that peritonitis may be a complicating factor It is not a purpose here to rob mesenteric thrombosis of its dramatic and catastrophic aspect but more to emphasize the fact that many patients do not have these features

Thus the most important features of mesenteric thrombosis are (a) Sudden pain across the upper abdomen This pain lacks the localization of other pains associated with special conditions as peptic ulcer and gallstones (b) Vomiting and distention of the bowel usually occur (c) Some degree of shock may be present in severe cases

but it is often absent unless a considerable portion of the bowel is involved (d) Fever is usually not present in the early stages but may come on two or three days after onset when bowel gangrene sets in (e) Although distention is a prominent feature muscular spasm is usually absent (f) Peristaltic rushes are absent (Fig 1)

Diagnosis The diagnosis of vascular occlusion is always difficult and frequently impossible to make Early diagnosis is important

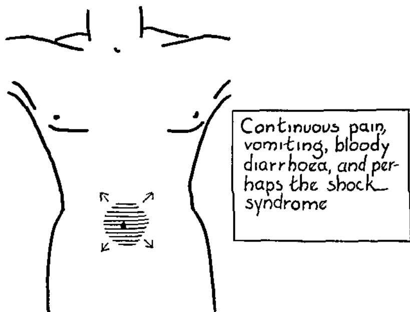


Fig 1—Mesenteric thrombosis Diagram showing area and distribution of pain in acute mesenteric thrombosis

because other diseases that may be helped by surgical intervention may be recognized and dealt with effectively Bowel obstruction peritonitis gallbladder disease perforating peptic ulcer with peritonitis and pelvic diseases must all be taken into consideration in differential diagnosis Mesenteric thrombosis is usually a disease of people past the middle period of life when arteriosclerosis is common Embolism however may occur in younger persons especially those with a vegetative endocarditis

Acute mesenteric thrombosis is often simulated by acute pancreatitis and is almost indistinguishable from acute bowel obstruction Many times genuine acute bowel obstruction is present in mesenteric

thrombosis Absence of a high fever and abdominal muscle rigidity are two points in differentiation Since the differential diagnosis of mesenteric thrombosis is often impossible before operation the physician s responsibility is to recognize the possibility of mesenteric thrombosis and the need of surgical intervention

TREATMENT

The treatment of mesenteric thrombosis is surgical rather than medical When there is acute abdominal pain and bloody diarrhea an operation should be performed with the hope that an early resection of a small loop of bowel may be sufficient to save the patient s life However measures must be carried out to combat shock and sustain the patient in the crisis

1 Intravenous injections of 1000 cc of ten per cent glucose in normal saline are helpful but blood or plasma transfusions are better

2 An opiate morphine sulfate 0 016 Gm (¼ grain) or pantopon 0 02 Gm (⅓ grain) hypodermically is necessary for pain

3 Sometimes the administration of oxygen is helpful

REGIONAL ENTERITIS

Since Crohn and Ginsburg first described this condition in 1932 there has been considerable interest manifested in regional enteritis but little has been added to our knowledge of this disease *It is a condition which in its acute phase must be differentiated from acute appendicitis and other acute inflammatory lesions of the right lower quadrant*

Etiology The etiology is unknown The most promising hope lies in finding an agent that causes obstruction of the mesenteric lymphatics To date infection has not been proven an etiologic factor

Pathology *The gross appearance varies with the stage of the disease* Roughly the condition is divided into the acute and the chronic phases In the acute phase the mesentery is so swollen and edematous that the bowel seems to sink into the mesenteric fat The bowel itself is thickened red lusterless and covered with plastic exudate The process is most commonly found in the terminal end of the ileum and often stops abruptly at the ileocecal valve However it may exist in

any part of the gastrointestinal tract from the duodenum to the rectum Several segments of the bowel may be involved with intervening areas of normal tissue In the chronic stage the muscular layer is markedly thickened and the lumen of the gut is narrowed The marked redness of the acute phase fades to a purple brown

Microscopically there are chronic inflammatory changes with occasional giant cells

Signs and Symptoms The disease is commonest in the young with the predominance in females being two to one In the acute phase the symptoms are similar to acute appendicitis with nausea vomiting and localization of pain in the right lower quadrant Tenderness and rigidity are present in this region and a mass may be palpable In the chronic stage the chief symptoms are pain and changes in the bowel habits of the heretofore regular patient Masses may or may not be palpable

Diagnosis In the acute phase the diagnosis is usually made at the operating table In the chronic phase gastrointestinal x rays carefully done will show areas of the gut in which the lumen is markedly narrowed This is known as the string sign On fluoroscopy the motility of the barium is carefully watched in the terminal ileum and any area showing abnormal mobility should be suspected Boon has advised introducing a Miller Abbott tube down to the lesion and then administering the barium through it in order to minimize the amount of barium necessary for fluoroscopy Any case suspected of having regional enteritis should have complete gastrointestinal x rays including a barium enema to rule out the possibility of several areas of the gut being involved with intervening normal tissue

TREATMENT

The accepted form of treatment has been surgical resection of the involved area together with wide sections of normal tissue on either end

It has been realized however that the acute phase may end in spontaneous regression and therefore some men advocate conservative treatment in this stage

There is no certainty that wide resection will prevent the condition from occurring in other segments of the bowel and therefore the prognosis should always be guarded

ULCERATIVE COLITIS

Ulcerative colitis is a disease of the large intestine characterized by inflammation and ulceration It may be acute or chronic with acute exacerbations Acute ulcerative colitis sets in abruptly often with sudden pain resembling that of acute appendicitis The etiology is still undetermined and there is a question as to whether the disease is a distinct entity It usually begins in the rectum and moves upward across the transverse colon often reaching the cecum The importance of making a diagnosis in the early phase of the disease cannot be stressed enough since prompt treatment may result in cure while without treatment the patient will probably pass from the acute stage into the chronic The disease may be fatal in the acute phase

Etiology Many different agents have been proposed as the cause but no agreement has been reached as to a single etiologic factor *However it is generally believed that the disease is infectious in origin* Hurst suggested that it was due to an unknown organism which was closely related to the Bacillus dysenteriae since it was similar to bacillary dysentery Rankin Bargen and Buie believe the disease is of bacterial origin and that the primary exciting factor is the diplo streptococcus They found that infected teeth tonsils and other foci of infection have preceded cases of ulcerative colitis, and that removal of foci of infection may cause a temporary flareup Allergy may play a definite role in etiology since many cases which have not responded to other forms of treatment have been benefited by management based on this hypothesis Systemic changes in the body alone or in conjunction with other factors may be responsible for ulcerative colitis Endocrine disturbances too have been suggested as causative agents Infection with gonococci tubercle bacilli streptococci, or other organisms may play a role in etiology as well as vitamin or other deficiencies Mental and nervous disorders *also play a part* Ulcerative colitis has followed severe streptococcic infections associated with chronic nephritis tonsillitis or acute rheumatic fever

Signs and Symptoms Patients with ulcerative colitis as a rule are in the second to fourth decades of life Symptoms are not always clear-cut Frequently the onset is abrupt and nausea weakness, fever and a bloodless diarrhea are commonly noted However there may

be constipation or no change in bowel habits Often the tongue has a white furred appearance which disappears as the disease progresses The acute episode may end fatally in a short time or it may subside only to flare up again later in milder or more severe attacks until the typical picture of chronic ulcerative colitis is evident

At times the disease begins in a gradual and progressive manner with mild diarrhea to which complaint the patient may pay little attention The diarrhea gradually grows worse the patient becomes weak and blood and pus appear in the stools The patient loses weight as a result of anorexia and diarrhea This marks the beginning of the chronic stage of ulcerative colitis Patients with chronic ulcerative colitis present a characteristic history of frequent intractable rectal discharges of pus blood and mucus mixed with feces The character of the stools is dependent on the severity of the disease and the degree of intestinal involvement Cramps and distress from gas or pain in definite regions such as starting in the upper left part of the abdomen and working down to the left thigh or along the course of the large intestine are common symptoms The patient has a drawn expression and the complexion is of a peculiar grayish yellow color

Premonitory signs of an acute exacerbation include malaise general exhaustion fatigue and a pulling sensation in the abdomen Aches and pains are felt over the entire body and small sores may appear in the mouth The clinical course of the acute form is usually comparatively short and stormy The disease may be highly toxic and fulminating with a fatal termination in two or three weeks or the patient may recover in from two to six weeks On the other hand the disease may become chronic and continue for months or years punctuated by periods of remissions and exacerbations

Diagnosis The classical picture of ulcerative colitis with fever malaise chills weakness sweating and prostration may make diagnosis comparatively easy However it must be differentiated from such acute diseases as typhoid fever and amebic or bacillary dysentery It is important to distinguish it from amebic dysentery by continuous and careful examinations of the stools for ameba and ova Carcinoma or tuberculosis of the bowel and other granulomatous diseases of the colon must also be considered before the diagnosis of ulcerative colitis is made

The five main diagnostic aids are

1 History
   a The patient has a diarrhea which causes little distress but which does not respond to home remedies A few weeks later a bloody diarrhea develops This history of blood in the stools especially in patients between the ages of 20 and 50 years is important in diagnosis
   b Usually pain of the crampy type is felt on both sides of the abdomen *Sometimes it is generalized at first and then localizes in the left lower quadrant*
   c Anorexia as well as loss of weight are outstanding features
   d Fever of the septic variety points to an active infection
   e Exhaustion is out of proportion to the other symptoms
   f The patient acquires a muddy gray pallor
2 Digital or rectal examination often serves to disclose tender ulcerated areas About 90 per cent of all cases of ulcerative colitis start in the rectal portion of the large bowel
3 Proctoscopic examination furnishes conclusive evidence of ulcerative colitis *showing typical ulcerations of the bowel*
4 X ray examination often shows a characteristic feathery appearance of the bowel It may reveal the extent of involvement and degree of destruction
5 Other diagnostic aids include gastric analysis stool and blood studies bacteriologic and parasitologic examinations and observations as to allergy and deficiency states

The complications of ulcerative colitis include severe and prostrating hemorrhages and multiple abscesses throughout the bowel Perforation with peritonitis sometimes causes a fatal outcome

Prognosis Formerly the prognosis was looked on as very unfavorable because few patients recovered but within recent years the mortality rate has decreased to about ten per cent This reduction is probably due to more accurate and prompt diagnosis since the disease is amenable to treatment if discovered early Most cases are subject to recurrence but if the episodes are treated promptly by complete bed rest and other measures the attacks become less severe and eventually cease in the majority of patients

TREATMENT

1 Complete bed rest is essential until all signs of inflammation disappear

2 Small blood transfusions of 300 to 400 cc should be given several times a week

3 An understanding of the pathological lesions reveals that food

with a high residue throws a burden on the involved large bowel The diet must be of a character that will lessen this load as much as possible A low residue high caloric (3000) and high protein diet is advised The utilization of vitamins is important yeast or vitamin B tablets and large amounts of vitamin C in divided doses are recommended It is necessary to educate the patient as to the importance of eating the tray should be attractive with small portions of food appetizingly prepared

4 Large doses of calcium in the form of lactate or gluconate 2 to 4 Gm (30 to 60 grains) daily orally or calcium chloride 10 cc of a five per cent solution may be injected intravenously slowly Many observers believe that ulcerative colitis is associated with a defective calcium metabolism

5 Paregoric may be given in doses of 1 33 to 2 00 cc (20 to 30 minims) three times a day to control the debilitating diarrhea Bismuth subnitrate 1 33 to 2 Gm (20 to 30 grains) three times a day may also be of value Tincture of iodine 0 33 to 0 53 cc (5 to 8 minims) in a glass of water on a full stomach or some iodine preparation is of aid in 15 to 20 per cent of cases

6 Dilute hydrochloric acid 1 33 to 4 cc (20 to 60 minims) in a glass of water may be taken with and after meals to combat the achlorhydria often associated with ulcerative colitis

7 Anemia especially the lowered hemoglobin content of the blood is an outstanding feature to be remedied Iron and ammonium citrate 1 Gm (15 grains) three times daily should be given Intramuscular injections of liver extract 2 to 3 cc twice weekly are also valuable therapeutic aids

8 Bowel irrigations with antiseptic solutions have been recommended Experience teaches us that physiological saline is as good an irrigating fluid as any

9 The sulfonamide drugs have been recommended in addition to the general treatment and satisfactory results have been obtained from their use in some cases Neoprontosil 0 33 Gm (5 grains) t i d has been the drug of choice since it is less liable to produce toxic reactions than the other drugs and at the same time it is equally effective However sulfanilamide has been used with comparatively good results Sulfaguanidine and more recently sulfasuxidine have been receiving favorable reports in the literature

10 *Specific Treatment* The concentrated serum seems to be most effective in controlling the acute phase which frequently clears up rather promptly on administration of injections twice a day for three to six weeks The dosage varies with the patient and with the severity of the disease The concentrated serum is usually given intra muscularly The first dose consists of a few minims this amount is increased by one minim per dose until 1 or 2 cc are administered daily Sometimes the disease is so acute that the patient must be given fairly large sized doses intravenously Usually the serum treat ment combined with the other therapeutic measures already men tioned brings the disease under control but this does not mean that treatment is finished The patient must observe a rigid routine of diet and medication for at least a year after release from the hospital After several weeks of serum treatment the administration of vaccine is begun It may be given twice a week subsequently once a week and later the intervals are lengthened until the patient receives a dose of vaccine every month for a number of months The initial dose is 1/10 cc which is increased in increments until the patient is being given 1/2 cc as often as necessary Persistence is the most impor tant part of the treatment The patient must not discontinue therapy when he feels quite comfortable and the acute phase is under control early cessation of treatment will probably result in recurrence which is more difficult to clear up than the initial attack

11 Surgery is indicated in cases of the fulminating type perfora tion or repeated hemorrhages of the colon abscess or fistula forma tion acute intestinal obstruction and complicated cases Patients with intractable symptoms which are not considerably improved after a course of medical treatment are candidates for surgery Ileos tomy with a follow up colectomy if necessary is the usual surgical procedure employed

HEMATEMESIS

Hematemesis or vomiting of blood is among the most important medical emergencies encountered since prompt and adequate man agement is necessary to save the life of the patient

Etiology Acute or chronic peptic ulcer is the commonest cause of hematemesis approximately one third of patients have hemateme sis during the course of the disease Peptic ulcer cirrhosis of the liver

and carcinoma of the stomach are the main causes of profuse hematemesis but there are many other conditions that may occasionally produce hemorrhage as jaundice acute hepatitis acute gastritis infectious diseases and trauma

Confusion may arise in the diagnosis when blood from the nose or lungs is swallowed and then vomited A careful history complete physical examination and a few simple tests as studying the specimen for tubercle bacilli are usually sufficient to determine the cause of hematemesis

Signs and Symptoms The blood may be either clotted or fluid and the color varies though it is usually dark The color of the blood is dependent on the length of time it has been in the stomach and the amount of acid in the gastric juice Vomiting of blood causes anemia with its consequences and there may be slight fever Sometimes edema develops Occasionally syncope or convulsions occur Hematemesis is often the first sign of an acute ulcer If the patient is first seen in a state of collapse after a severe hemorrhage he is pale the pulse is rapid and thready the blood pressure is reduced and the skin is cold and clammy

Diagnosis Hematemesis must be differentiated from hemoptysis but this is not usually difficult The history of previous bleeding from the lung evidence of tuberculosis or heart disease precede hemoptysis while in hematemesis a history of cirrhosis of the liver gastric disturbances or previous hematemesis is obtained In hemoptysis the blood is bright red frothy and mixed with mucus and it is ejected after a tickling sensation in the throat in hematemesis the blood is usually dark in color unless the hemorrhage is profound and has an acid reaction

If the patient is not seen during the attack difficulty in diagnosis may arise Some hysterical patients swallow blood and then eject it or more often they consume wine juice of cherries or strawberries or some red-colored fruit which stains the vomitus so it looks like fresh blood others take iron bismuth and bile which give the blackish color of altered blood Examination of the vomitus for blood will clear up this confusion

Prognosis Prognosis is favorable though when bleeding is caused by cirrhosis of the liver or if the patient with a peptic ulcer is past 50 years of age the outlook is grave When the patient is over 50

years arteriosclerosis is common and the ulcerous lesion may open into a hardened artery which fails to contract, and hemorrhage may be fatal In younger individuals the elasticity and resiliency of the artery are preserved and clotting tends to occur It should be remembered that a patient who is hemorrhaging may die despite the best of care This is particularly true when the bleeding is from a ruptured esophageal varix perforated aneurysm or from an ulcer which involves the pancreas

The severity of the hemorrhage and the underlying cause are the chief factors in prognosis However other elements are important too as the ability of the individual to withstand hemorrhage, the general state of health at the time of hemorrhage and the precision and care used in management While the blood counts and the reduction in blood volume are indicators of the degree of hemorrhage it is the pulse rate blood pressure and response to transfusions that reveal how well the patient tolerates the loss of blood

TREATMENT

The main principles in treatment are to keep the patient quiet and to maintain adequate blood volume by means of intravenous fluids and transfusions In the early stage, the patient should be made comfortable by means of sedation After the state of collapse subsides and the pulse becomes slower and stronger usually within an hour the patient may be moved to a suitable place for treatment He should not be moved when he is in a state of shock because it may cause immediate death

1 The patient should be put to bed as soon as possible with his head lower than his feet Heat may be supplied to the body in the form of blankets and hot water bottles Absolute rest is required and is attained by the administration of morphine sulfate 0 016 Gm (¼ grain) or more with atropine sulfate 0 45 mg (1/150 grain) hypodermically nembutal 0 39 Gm (6 grains) chloral hydrate 0 19 Gm (3 grains) or sodium bromide 2 Gm (30 grains) may be given by rectum The patient with hematemesis usually is terror stricken sedation should be repeated as often as necessary to keep these individuals in the twilight zone of consciousness If the hemorrhage is due to cirrhosis of the liver morphine should be withheld or given in minute doses because the detoxicating power of the

liver may be diminished so that 0 016 Gm (¼ grain) morphine may be harmful

2 Nothing should be given by mouth for a day or two though the mouth may be rinsed out with water from time to time and ice chips given

3 A blood count must be done and the hemoglobin percentage estimated immediately These are of value in that they show the degree of hemorrhage though the blood count cannot always be relied on because it may appear higher than it really is due to dehydration or hemoconcentration This is especially true immediately after hemorrhage has occurred and before the blood volume has been restored by transfusions and intravenous fluids

4 The blood must be typed and a donor secured in case an emergency transfusion is necessary Blood transfusions are required if the hemorrhage continues Between 100 and 200 cc may be given at intervals of one to two hours

5 An attempt is made to restore the blood volume by administering saline or glucose intravenously or saline and tap water by rectum These fluids must be given slowly The condition of the patient is improved by the intravenous administration of 1000 to 2000 cc of five per cent glucose in normal saline daily in most cases but some clinicians believe fluids promote the hemorrhage However if the blood volume is maintained 2 000 000 red blood cells are sufficient to carry on proper oxygenation of the tissue throughout the body and fluids should not have an ill effect

6 The blood pressure should be taken immediately and every two hours thereafter until the crisis is over The pulse rate should also be determined every two hours A rapid thready pulse usually means the hemorrhage is continuing whereas a slower rate indicates that the patient is tolerating the hemorrhage well

7 Thromboplastin 20 cc intravenously or some like substance may aid coagulation More rapid clotting of the blood may also be obtained by an intramuscular injection of 10 cc of 10 to 20 per cent calcium gluconate every four hours for two to four injections

8 Cathartics and enemas are contraindicated

9 After the patient has improved sufficiently a diet routine may be started There is some controversy as to whether the patient should be fed immediately or not Recently Meulengracht s treatment has

been used whereby the patient is placed on a soft palatable diet imme diately However it is best to withhold food by mouth for 48 to 72 hours

10 If the hemorrhage is not controlled in three days by strict and adequate medical measures the surgeon should be given an opportunity to locate the bleeding vessel and ligate it The best sur gical results are obtained in patients with chronic ulcers because the ulcer is easy to locate and the diagnosis is more or less confirmed before surgery is undertaken

11 X rays should not be taken for several weeks because barium acts as a foreign body and may precipitate a recurrence of the hem orrhage It is much more important to stop the hemorrhage than to diagnose the cause

CHAPTER XVII

The Liver

JAUNDICE

Jaundice is due to an excessive amount of bile pigment in the blood and tissues of the body Unlike other secretions bile produces an intense discoloration of the tissues and its presence is promptly recognized

Etiology Jaundice like anemia is a condition that may be brought about by many different causes It is a sign found in a variety of diseases caused by abnormal conditions having little or no relation to one another The chief factors producing jaundice fall into three groups (1) Excessive hemolysis of the red blood cells as seen in acute or chronic hemolytic jaundice (2) obstructive lesions within or outside of the common bile duct and (3) damage of the liver cells themselves caused by toxic agents or infections commonly known as intrahepatic jaundice Rich has recently introduced a classification of jaundice based principally upon the urinary and stool findings and has subdivided it into retention and regurgitation types McNee recognized the three varieties of jaundice and introduced the following classification

1 Hemolytic
   a Acute
      (1) Due to acute infections as streptococcal infections typhoid fever Weil s disease and malaria
      (2) Phosphorus arsenic or other poisoning
   b Chronic
      (1) Congenital or familial
      (2) Acquired.
2 Obstructive
   a Gallstones catarrhal inflammation of the duodenum ampulla of Vater and common bile duct.
   b Carcinoma of the head of the pancreas.
   c Enlarged lymph nodes pressing the common duct from without as in carcinoma leukemia or Hodgkin s disease

3 Toxic or infective jaundice (otherwise known as intrahepatic jaundice)
 a Acute hepatitis leading sometimes to yellow atrophy and at other times to healing
 b Multiple abscesses of the liver
 c Sclerosis of the liver
 d Multiple carcinoma of the liver

Pathology The salient features in the pathology of hemolytic jaundice are illustrated in the accompanying diagram (Fig 1) and need not be further elucidated here

Obstructive jaundice is characterized by a regurgitation of bile back through the capillaries into the perivascular spaces whence it finds its way into the blood This produces a large greenish yellow liver, which later on in the course of the disease becomes nodular due to cirrhosis Microscopically, marked dilatation of the biliary canaliculi many of which contain bile thrombi, is noted Later on, there is fibrous tissue proliferation about the larger bile ducts with the occurrence of a mononuclear type of cellular reaction producing the characteristic picture of biliary cirrhosis

The pathology of hepatocellular jaundice is discussed in a later section of this chapter

Signs and Symptoms An attack of jaundice may be acute or chronic. It may come on abruptly, associated with fever chills general malaise and be merely a subsidiary event in the course of a serious and severe disease as acute streptococcal hepatitis or it may develop so imperceptibly without any other symptoms that the patient is considered more jaundiced than ill The urine may possess a definite greenish hue due to the presence of bile pigment the stools may be colorless and described as clay colored in obstructive jaundice However jaundice is usually recognized by the presence of the yellow pigmentation in the sclerae Other organs may also be involved for example the liver may be enlarged and tender the heart slower than normal and there may be a tendency toward capillary oozing throughout the body

Hemolytic jaundice also known as hemolytic anemia follows a rapid destruction of the red blood cells and occurs in the acute or chronic stages Acute forms are seen in connection with severe infections and sometimes after transfusions when there is a rapid destruction of the blood cells (Fig 1) Chronic hemolytic jaundice is

DIFFERENTIAL DIAGNOSIS OF JAUNDICE

DISEASE		CLINICAL FEATURES						LABORATORY FEATURES						
		P	W ght Lo	G I C m pl t	Fever	Cl y Sto l	D k Ur	I ter s I d x	V d B gh	B le U	U bl g U	U bl og F	L F t	P e e te E ym s U r d Blood
Obstructive Jaundice	Gall Stone	++++	0	+++	±	+++	+++	8 to 100 (20 to 60)	Direct	++++	0 to 6 mg (10 to 100 if there is associated liver damage)	10 to 500 mg	Normal (unless associated with liver damage)	Normal
	Cancer	±	++++	++	0	++++	++++	80 to 300	Direct	++++	0 0 to 0 3 mg	0 0 to 5 0 mg	Normal (unless late in disease or with metastases)	Increased (early)
Hepatic Jaundice		+++	+	+	+++	0 to +++	0 to +++	10 to 300	Direct or biphasic	+ to +++	8 to 400 mg	8 to 1200 mg	Impaired	Normal
Hemolytic Jaundice		0	0	0	0	Green	0	8 to 30	Indirect	0	1 to 3 mg (depending on liver function)	300 to 3000 mg	Normal	Normal

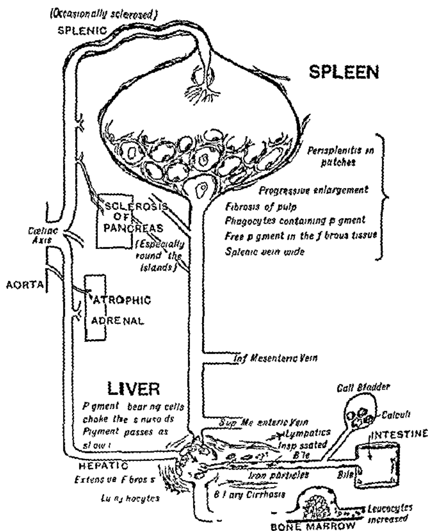


Fig 1—The chief changes in hemolytic jaundice (Moynihan's The Spleen and Some of Its Diseases W B Saunders Company)

usually not as serious as the acute type When a diagnosis of hemolytic jaundice is made the cause of the destruction of the red blood cells must be determined and removed

Obstructive jaundice in patients past the middle period of life is usually caused by gallstones in the common duct or by carcinoma of the head of the pancreas compressing the common bile duct Other conditions may have to be considered but only after these two commonest causes have been eliminated Lymph gland enlargement due to carcinoma leukemia tuberculosis or Hodgkin s disease may compress the common duct from without The diagnosis of obstructive jaundice due to gallstones is made essentially by a history of repeated attacks of colicky pain in the upper abdomen followed by periods of jaundice Gallstone disease almost always occurs in the middle period of life especially in women who are stout and who have enjoyed good health An x ray film is necessary to identify the gallstones In carcinoma of the head of the pancreas there is quite a different story The patient is usually beyond the middle period of life and has been in failing health for some time there is an associated loss of weight appetite and energy Jaundice usually comes later and is at first mild and hardly noticeable then there is an augmentation of the jaundice to a deep yellow type and finally a dark yellow or black jaundice develops Sometimes in the diagnosis of carcinoma of the head of the pancreas serum amylase and particularly lipase determinations may be helpful but frequently they are not

Intrahepatic or toxic jaundice involving the liver itself is the commonest type of all In this category are a number of different kinds of the disease For example there is what used to be commonly called acute catarrhal jaundice in which there was postulated a mild hepatitis with an extensive mucous inflammation of the ampulla of Vater or duodenum This term has been largely replaced by the designation infectious hepatitis particularly since experiences during the recent war have brought this syndrome to the fore It is generally conceded that a virus is responsible for this disease and these patients who are usually in the younger age groups complain most commonly of anorexia for several weeks gastrointestinal upsets fever and marked malaise The urine is frequently dark and shortly thereafter jaundice appears The incubation period of infectious hepatitis is generally considered to be from 2 to 5 weeks The lack of precise

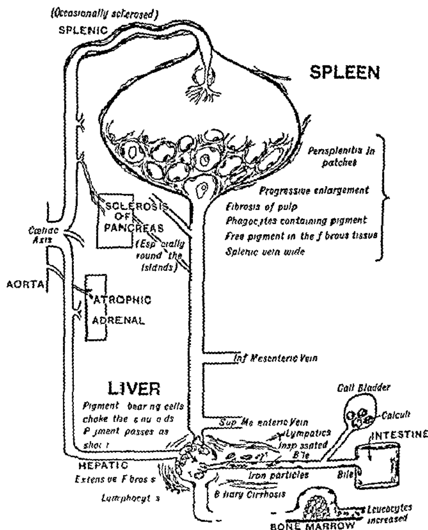


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knowledge as to how much liver involvement exists makes it difficult to give an accurate prognosis in these cases Sometimes this type of jaundice fails to heal in the usual two to four week period and in place of recovering the patient becomes worse and finally dies with an extensive destruction of the liver However infectious hepatitis is usually followed by prompt recovery within a three week period

Closely allied to infectious hepatitis is the entity described under the name homologous serum jaundice This type follows the administration of plasma and blood transfusions or inoculations of any kind but has a longer incubation period namely from 2 to 5 months The pathological changes associated with homologous serum jaundice cannot be distinguished from those associated with infectious hepatitis

Acute hepatitis may follow the taking of drugs as cinchophen salvarsan or such chemical poisons as impure alcohol When the poisoning is due to arsenic that metal may be recovered from the urine hair or nails The liver in acute hepatitis is enlarged and painful The patient is very sick Fever vomiting and sometimes convulsions are present As the condition becomes worse vomiting and diarrhea of blood and urinary suppression intervene If not relieved the patient becomes more toxic and irrational passes into a state of muttering delirium and finally enters the stage of deep coma which is followed by death

Diagnosis The diagnosis of jaundice is usually obvious but some confusion may exist from the poisons of carotinemia saffronemia or ochronosis Malingerers sometimes take saffron to simulate being jaundiced

After one has decided that the patient is jaundiced the method of approach in determining the kind of jaundice becomes the next step In general there are three important points (1) A careful history of the events leading up to the onset of jaundice to determine if poisons medications or serious infections may have provoked the attack Inquiry regarding exposure to cases of infectious hepatitis or the receiving of transfusions plasma or injections is important The age of the patient is of primary concern because young persons are apt to have infectious hepatitis or one of its varieties in the middle period of life gallstones are the commonest cause while in later periods of life carcinoma of the head of the pancreas must be con

sidered The associated complaints constitute guide posts in the differential diagnosis of jaundice for example a patient beyond the age of 50 years who has been in poor health for some weeks and gradually loses strength weight and appetite followed by a gradually deepening but painless jaundice is according to the law of averages very likely to have carcinoma of the head of the pancreas

(2) The examination of the patient Very often little can be obtained from the physical examination but there are notable excep

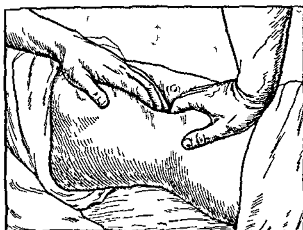


Fig 2—Palpation of the lower border of the liver (Gilbert s procedure)

tions The presence of chills and fever in a jaundiced patient may indicate such conditions as acute cholecystitis with acute cholangeitis epidemic infectious jaundice or abscesses of the liver following pyelophlebitis The enlargement of the liver may indicate abscess biliary cirrhosis or carcinoma of the liver Certain poisons particularly phosphorus produce a prompt enlargement of the liver with an abrupt onset of jaundice The physical examination must include careful palpation of the lymph nodes of the body as generalized carcinomatosis leukemia or syphilis may be associated with involvement of the biliary passages and pressure on the ducts from without causing jaundice Rectal examination for carcinoma must be done as there may be metastases to the liver or the lymph glands around the large bile ducts even before many symptoms are present from the rectal involvement itself Palpation of the abdomen may reveal a dis

tended painless gallbladder in a middle aged person or an older one that suggests carcinoma of the head of the pancreas Gallstones seldom cause jaundice and enlarged gallbladder

As a rule a precise history and a careful physical examination are all that are required to make a conclusive diagnosis of the cause of jaundice Sometimes the cause and kind of jaundice are not so obvious then we must resort to the third phase of investigation that is (3) the laboratory aids (a) As the hemorrhagic tendency in a jaundiced patient is of such outstanding importance to the examin

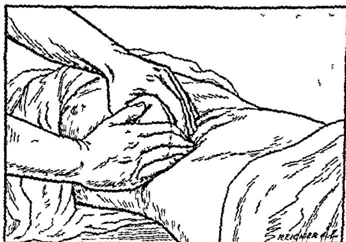


Fig 3—Palpation of the lower border of the liver (Mathieu s procedure)

ing physician the methods of determining the degree of the threat of hemorrhage will be discussed briefly The bleeding time and coagu lation time of the blood must be estimated Although normal figures for these tests do not eliminate from consideration the tendency to hemorrhage they are helpful The prothrombin deficiency in the blood may now be determined with considerable accuracy and this is the best index of the hemorrhagic tendency Vitamin K being a fat soluble vitamin in the natural state is dependent upon bile salts for absorption in the gastrointestinal tract as other fat soluble vitamins are In an obstructive jaundice vitamin K may fail to be absorbed As vitamin K is responsible to some degree for the prothrombin forma tion lack of vitamin K may cause bleeding then too the liver may be diseased and incapable of forming prothrombin from the vitamin K

(antihemorrhagic vitamin) The bleeding time and clotting time may be normal and yet prothrombin deficiency in the blood may be present A normal prothrombin time is from 11 to 12 5 seconds In jaundice it may be very greatly reduced and when it is 40 per cent of normal the patient is in the danger zone This is an important determination because it is a guide to the treatment To overcome the hemorrhagic tendency several preparations are now available which increase the prothrombin level of the blood to normal Such preparations are Synkavite and Synkamin These may be injected intra

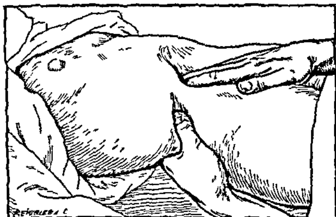


Fig 4—Palpation of the lower border of the liver (Glénard s thumb procedure)

venously or taken by mouth two or three times a day depending on the severity of the jaundice A test of liver function which depends upon the ability of the liver to respond to parenteral injections of vitamin K has been introduced In hepatocellular disease this response as measured by a decrease in the prothrombin time is impaired while in obstructive jaundice particularly in the early stages the response is present

(b) A plain x ray plate of the upper abdomen may reveal gall stones or a distended gallbladder Other x ray tests includes a careful gastrointestinal examination to eliminate carcinoma of the stomach and other lesions A dye test of the gallbladder may fail to give aid when jaundice is present but much information is sometimes obtained from the cholecystogram

(c) An icterus index is an indicator of the degree of jaundice and tells whether it is becoming more intense or less so before it can be determined in any other way The Van den Bergh test of the blood was introduced for the purpose of making a differentiation between hemolytic obstructive and hepatic types of jaundice While it does not give as precise information as was hoped for, the test is often a valuable aid in the differential diagnosis of jaundice

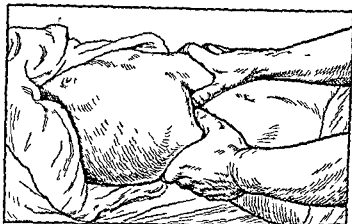


Fig 5 —Palpation of the lower border of the liver and of the gallbladder by the two-thumb procedure.

(d) A careful examination of the blood, including counts to exclude unusual cases of leukemia or anemia an estimation of the cholesterol content both total and fractional determinations and if possible a determination of the quantity of total protein and the albumin globulin ratio are important

(e) Examination of urinary and stool urobilinogen particularly by quantitative methods is especially helpful Frequently on the basis of this test plus the history and physical examination the diagnosis may be ascertained A positive urobilinogen test of the urine usually indicates jaundice with liver damage while a negative test points to an obstruction due to carcinoma or stone extrahepatically Reduced quantities of urobilinogen in the stool will indicate an obstructive type of jaundice while the highest values in this determination are found in hemolytic jaundice

(f) Liver function tests may be carried out in less acute and less obvious cases of jaundice for example the intravenous galactose test

the hippuric acid test and the simultaneous determination of either the cephalin cholesterol test or the thymol turbidity test and the alka line phosphatase test may be very helpful in determining whether the liver damage is an important contributory factor in the presence of jaundice

TREATMENT

The treatment of the jaundiced patient depends almost entirely on what kind of jaundice the patient has If it is due to toxin the

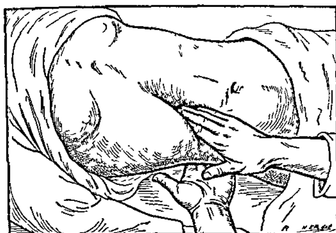


Fig 6—Bimanual palpation of the liver The physician stands at the right of the patient His left hand with the thumb free and fingers together is applied transversely behind the flank against the last rib His right hand pressing in the abdominal wall hooks about the liver and palpates it The physician is thus en abled to appreciate the size consistency shape and mobility both of the right lobe of the liver and of the gallbladder (Letulle)

elimination of the toxin is the important thing If due to obstruc tion this must be overcome usually by surgical means If due to a lesion in the liver itself therapeutic measures must be directed at the prevailing condition

Notwithstanding the cause of jaundice the following general measures may be helpful

1 Intravenous glucose 1000 cc of ten per cent solution once or twice a day

2 Intramuscular injections of vitamin B in doses of 10 000 to 20 000 units every day or two

3 A high carbohydrate high protein low fat diet

4 Alkalinization with usual measures

5 Bowels are kept active with magnesium preparations, as magnesium oxide 0 66 to 1 Gm (10 to 15 grains) three times a day following meals or milk of magnesia 15 cc (½ ounce) daily Simple saline enemas may give relief

6 If severe pain is present morphine sulfate 0 016 Gm (¼ grain) and atropine 0 005 Gm (1/120), or pantopon 0 022 Gm (⅓ grain), should be given hypodermically These drugs may be repeated within an hour if indicated

7 Calcium chloride 20 cc of a five per cent solution given intravenously slowly may bring relief Calcium gluconate or calcium lactate 1 Gm (15 grains) should be given three to four times daily

8 Viosterol 20 drops every two hours until six doses have been given then 30 to 60 drops three times a day should be administered

9 Vitamin K should be given prophylactically particularly if surgery is contemplated even if the prothrombin content of the blood is normal If the prothrombin content of the blood is low the dose should be 10 20 mg (1/6 to 1/3 grain) daily If oral therapy is not feasible it may be administered intramuscularly in the dose of 5 to 10 mg (1/12 to 1/6 grain) A single dose thus administered is effective for several days to a week

10 Calamine lotion with one per cent phenol frequently applied locally may afford some relief for the intense itching

11 In the event ascites is present abdominal paracentesis is advisable This procedure should be followed by administration of diuretics as salyrgan 1 cc (15 minims) given intravenously every other day for three doses or ammonium chloride 2 Gm (30 grains) three times a day may be given for a period of five days

ACUTE HEPATOCELLULAR DISEASE

Acute hepatitis is an acute inflammatory or degenerative disease of the liver The malady is divided according to the degree and severity of the syndrome infectious hepatitis formerly known as acute catarrhal jaundice usually being of a mild degree a type of intermediate severity which may be a progression of the first type and which also is occasionally caused by metallic poisoning and the stormy dramatic syndrome of acute yellow atrophy

Etiology The etiology of hepatitis may be chemical infectious

or metabolic The known causes of chemical nature are chloroform phosphorus trinitrotoluene arsenic, mercury, cinchophen carbon tetrachloride and sulfonamide drugs The sulfonamide group of drugs has proved a particularly important etiological factor Carbon tetrachloride may exert its noxious effect through inhalation over a long period of time Infections which are of etiological importance are the common cold influenza syphilis spirochetosis ictero hemorrhagica and amebiasis In cases associated with syphilis it is often difficult to determine whether syphilitic infection or the arsphenamine therapy has damaged the liver parenchyma There is some evidence that cases of so-called postarsphenamine jaundice were in reality cases of syringe transmitted viral hepatitis There are cases reported in which the jaundice of the early stage of syphilis developed into acute yellow atrophy without the administration of arsphenamine Metabolic states at times associated with hepatitis are pregnancy and hyperthyroidism

Pathology There is apparently a close relationship among infectious hepatitis intermediate or moderately severe hepatitis acute yellow atrophy and cirrhosis The difference is one of severity of injury and of chronicity The milder cases recover after an illness of weeks or even months and are classified as infectious hepatitis If the jaundice becomes more severe and terminates fatally acute yellow atrophy is recognized

The basis of infectious hepatitis may be thought of as a viral infection of the liver involving both the polygonal cells and the bile ducts Biopsy shows cloudy swelling of the parenchymal cells and compression and inflammation of the small bile ducts and of the gall bladder Necrosis of the liver cells is produced by the virus involved and in other cases by chemical or perhaps bacterial toxins The bacteria of bacterial toxins are seldom found in the liver The poisons of disordered metabolism form an important group These poisons are carried to the liver to be destroyed and the liver cells often perish in the attempt In Weil s disease the liver merely shows cloudy swelling but it contains large numbers of spirochetes There may be associated necrosis of the renal tubules

The liver in acute yellow atrophy is atrophic and yellow It may be half its normal size At first the organ is bright yellow later it becomes red as the necrotic cells disappear The usual appearance

at autopsy is a mottling of red and yellow areas The kidneys are apparently acted upon by the same toxin which destroys the liver and the epithelium of convoluted tubules may show marked necrosis The urea excreted is greatly diminished as it is no longer formed by the liver The amino acids are correspondingly increased as the normal de amínization which occurs in the liver is stopped The end picture of acute yellow atrophy with recovery is one of hyperplastic nodules of liver cells separated by an abundant connective tissue containing large numbers of bile ducts

Signs and Symptoms The onset may be insidious The symptoms are varied For several days or weeks there is marked anorexia this being probably the most outstanding complaint Also noted are malaise nausea occasional vomiting and constipation or diarrhea Fever of 37 8° to 38 3° C (100° to 101° F) is seen in patients After a latent period of 1 to 2 weeks or so jaundice appears and becomes deeper the stools may become acholic and the urine often contains bile Mental sluggishness pruritus and general lassitude are characteristic of this period There may be bradycardia The liver may be enlarged and tender The gallbladder and spleen are sometimes palpable As jaundice becomes more marked the digestive disturbances may become less severe although they frequently persist if untreated

Drug intoxication with hepatitis may be accompanied by the symptoms of the effect of the drug on other organs or systems Should the patient live two or three days evidence of hepatic damage appears as does enlargement and tenderness of the liver and at times of the spleen Anorexia epigastric distress nausea and vomiting are associated Jaundice is frequently present

Acute yellow atrophy remains benign for a period of days or weeks The second stage however is abrupt in onset Severe headache restlessness delirium vomiting convulsions transient paralysis and dilatation of the pupils are indicative of marked toxemia and irritation of the nervous system The jaundice becomes deeper the liver begins to diminish in size hemorrhages may occur into the skin or from mucous surfaces The temperature usually remains low but may rise suddenly before death The disease almost always proves fatal in a few days after onset of the severe symptoms and usually after the development of coma and stertorous breathing

Diagnosis Recent investigators have agreed that a decrease in the amount of prothrombin in the plasma is the most probable explanation of the hemorrhagic tendency in jaundice The maintenance of a normal prothrombin value is determined by the presence in the food of an adequate supply of vitamin K and in the bowel of sufficient bile for absorption of vitamin K The prothrombin content of the blood is decreased after experimental hepatic injury and in some cases of cirrhosis and severe hepatitis For this reason determinations of the prothrombin time will often shed light on the diagnosis and the administration of vitamin K may be begun if indicated

Slight elevation of the serum phosphatase may be of value as a means of indicating early liver damage in cases under treatment with neoarsphenamine Syphilis *per se* does not elevate the blood plasma phosphatase Early detection of an arsenical hepatitis is essential if severe grades of inflammation are to be avoided The serum Van den Bergh reaction is direct or biphasic The icterus index varies widely As a rule the higher the icterus index the more severe the disease and the greater the possibility of transition to acute yellow atrophy Frequently the flocculation tests are used in conjunction with the serum alkaline phosphatase determination to determine hepatocellular disease The former are strongly positive and the latter normal in these cases The galactose tolerance test is also useful in the diagnosis of recent hepatocellular injury

It should always be borne in mind that liver function tests do not establish the differential diagnosis in any case and are only of confirmatory value It is generally recognized and has been pointed out by many prominent investigators in this field that in the differential diagnosis of jaundice the procedures which are of the greatest value are the history and physical examination

At the outset of catarrhal jaundice the urobilinogen of the urine is elevated This is an almost invariable finding thus emphasizing the importance of this determination early in the course of the disease to establish the proper diagnosis As the jaundice deepens the amount rapidly decreases because bile is now largely excluded from the bowel and little urobilinogen is being formed and absorbed into the portal circulation During this period the feces bile and urobilinogen are markedly reduced The reappearance of an increased amount of

urobilinogen in the urine is often the first evidence of improvement The amount in the feces increases very rapidly Persistent elevation of the urine urobilinogen in spite of the disappearance of jaundice should warn that liver damage still exists and that recurrence of jaundice may take place This has been noted in cases of acute hepatitis which smoulder and then flare into acute yellow atrophy

The leukocyte count is normal or decreased A macrocytic anemia may occur in the more severe and prolonged cases In the severe and terminal cases nitrogen retention with uremia may complicate the cholemic picture already present

Prognosis Prognosis in acute yellow atrophy is grave and that of all forms of hepatitis is guarded

TREATMENT

1 Bed rest is essential in all cases of hepatitis until convalescence is well established

2 Fluids should be forced

3 The diet should be high in carbohydrate high in protein and low in fat At least half the carbohydrate should be given as glucose Intravenous ten per cent glucose is advisable in quantities from 500 to 1000 cc daily even though the patient does not vomit

4 If sedation is required a combination of barbiturates salicylates and codeine is effective in small amounts and over short periods of time The more potent opiates are not tolerated well where liver damage is present

5 Vitamin B in large doses 10 000 to 20 000 units intramuscularly is recommended

6 Magnesium sulfate solution is advised on a fasting stomach every four or five days Magnesium sulfate 15 to 30 cc (½ to 1 ounce) may be given by mouth daily for catharsis if necessary

7 Sodium thiosulfate in doses of 0 5 Gm (7½ grains) intravenously two or three times daily is useful in rendering heavy metals insoluble and so retarding or preventing their absorption Sodium formaldehyde sulfoxylate in doses of 10 Gm (150 grains) intravenously daily is thought by some clinicians more effective in preventing the absorption of such metals

8 Ferrous salts may be necessary to combat the anemia Antipruritics vary in their efficacy and may be left to individual selection

9 The use of lipotropic substances such as choline and methionine has been advocated in some quarters There is question however as to their effectiveness

10 Crude liver extract frequently appears to be of benefit This preparation is given intravenously after dilution with normal saline solution in gradually increasing amounts until 10 to 20 cc three to four times a week are given

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CHAPTFR XVIII

Acute Infections

FEVER, PERSISTENT AND OBSCURE

Occasionally fever constitutes the only evidence of a disorder until the disease has run almost its entire course It is readily granted that *the term obscure fever is a relative one for what may be obscure* fever in one locality may be quickly explained in another where more careful work is done The term obscure fever should be reserved for the cases of long continued fever in which careful and skillful examinations have been performed and yet the fever remains unexplained

Etiology After painstaking history and physical examination have been completed and the usual laboratory tests made, a certain number of cases will remain undiagnosed The following diseases are the commonest causes of a persistent unexplained fever (1) Tuberculosis (2) subacute bacterial endocarditis (3) carcinoma of internal organs (4) thrombophlebitis (5) rheumatic infection and (6) a hidden septic focus Typhoid fever, undulant fever, syphilis and *malaria may confuse one for a while* but the special tests clear up the diagnosis

Diagnosis Before a diagnosis of obscure fever is made the history should be carefully studied and a searching physical examination must be done The aches and pains mentioned by the patient should be considered as well as his habits and occupation The character of the fever and mode of onset are often of aid in arriving at the diagnosis and determining the cause

The approach to the special studies is outlined as follows

1 Blood culture
2 Throat sputum urine and stool cultures
3 X rays of the chest
4 Agglutination studies
5 Rectal examination especially if malignant disease is suspected

6 Erythrocyte sedimentation test
7 Radiography of the alimentary canal

The blood throat sputum urine and stool cultures often reveal the causative organism as the streptococcus staphylococcus or tubercle bacilli Tuberculosis should always be suspected an x ray examination showing a shadow at the apex of one lung with the associated symptoms of cough and loss of weight points toward tuberculosis unless another diagnosis can be positively made The Widal test usually discloses typhoid and the agglutination tests for tularemia undulant fever typhus and Rocky Mountain spotted fever are equally revealing

Failure to recognize the cause of the fever may be attributed to the atypical onset and course of the disease the disease may not be well known or it may not come to mind because of its rareness in the locality characteristic symptoms may not be present or they may be present for too short a period of time or examinations may be inaccurate or carelessly done

Concealed suppurative processes as empyema abscess in the mediastinum perinephritic abscess and pararectal collection of pus may be difficult to diagnose The exploratory needle employed to make diagnostic chest taps is the instrument that has explained more unexplained fevers than any other Notwithstanding x ray and other examinations percussion of the chest occasionally suggests the presence of loculated pus and the diagnostic tap reveals it After a painstaking examination has been made tuberculosis subacute bacterial endocarditis and thrombophlebitis should be considered An early carcinoma of a parenchymatous organ as the kidney liver or spleen may escape diagnosis until late in the course of the disease

CHICKENPOX (VARICELLA)

Chickenpox is an acute communicable disease characterized by eruptions of papules in various stages of evolution

Etiology The infectious agent is a filterable virus entirely distinct from the virus of smallpox but having some relationship to the virus of herpes zoster The disease is usually a childhood illness leaving a lifelong immunity but adults who have not contracted this illness in childhood remain susceptible The causative agent is air

borne and may also be spread by droplet infection entering the body through the mouth and nose

Pathology The superficial layers of the skin are involved though in exceptional cases there may be involvement of the corium Since the outer layer of epithelium is implicated pock marks or cicatricial changes are exceptional unless *secondarily infected* The pathological changes are limited to the skin and mucous membranes

Signs and Symptoms The incubation period varies from 4 to 21 days but it is exactly 14 days in most cases Rarely is the disease ushered in with a convulsion It usually starts with fever for approximately 24 hours with a continuance of the fever throughout the eruptive stage The eruption starts on the face and torso It has a tendency to exaggerate the number of lesions on the covered parts of the body while the number on the extremities is less The lesions hastily go through a transition of the macular to the papular stage and rather rapidly fill with a transparent, and exceptionally a translucent fluid The lesions are conglomerative or heterogeneous in character *i e*, *a given area will present lesions in the papular, vesicular* and desiccating stages After approximately three to five days of fever and eruption a normal temperature and a desiccation period of seven to ten days follows The lesions are usually discrete Very rarely will a malignant type (varicella gangrenosa necrotica) occur

Complications Chickenpox may be complicated by *secondary* infections of the skin, resulting in abscesses furuncles or erysipelas The lesions may be malignant by their position in the larynx cornea of the eye or within the urethra Occasionally encephalitis may be a complication

Differential Diagnosis Smallpox with its three to five day prodromal period and subsequent eruption is the most important disease in differentiation Secondary pustular syphilis with its positive history and serological examination are readily ruled out Secondarily infected scabies are easily recognized by their lack of eruption on the face and the intense pruritus at night Pustular dermatoses dermatitis herpetiformis and impetigo are sometimes confused

Prognosis *In the average case of chickenpox a prompt* recovery may be predicted within two weeks unless severe secondary infections occur Patients should be warned that if pocks become infected and are scratched off scars may persist for years

TREATMENT

1 Institutional vaccination for this disease has been tried but is not of practical usage Pooled convalescent serum given intramuscularly in 10 cc dosage during the first five days after exposure will generally either result in complete protection or so alter the infection that there will be very few vesicles and practically no febrile reaction Chickenpox is a reportable and placardable disease

2 The patient should rest in bed until the lesions are past the acute stage and the temperature is normal for a few days

3 Weak potassium permanganate tub soakings act as an antiseptic and alleviate the itching of the lesions The crusts should be removed with ointment as ointment of ammoniated mercury only after complete desiccation has occurred

4 In the presence of fever a light diet is given

5 The only danger in the disease is secondary infection of the lesions To prevent this special attention to general cleanliness is imperative

WHOOPING COUGH (PERTUSSIS)

Whooping cough is an acute communicable disease involving the upper respiratory tract and characterized by spasmodic attacks of coughing terminating with an inspiratory whoop

Etiology The most likely cause of whooping cough is the Bordet Gengou bacillus although the virus has been commented upon as a symbiotic cause of infection Bacteriologically the bacillus has been demonstrated as being essential to the occurrence of the disease The disease is spread by means of cough droplets by direct contact and is considered quite definitely air borne for short distances

Pathology The blood picture in most cases presents a most marked leukocytosis with a differential picture of high lymphocytes The trachea bronchi and bronchioles are greatly inflamed during the early or catarrhal stage of the disease At first the mucus secreted is not very thick but later it becomes semiviscid and stringy and accumulates Some authorities believe this accumulation irritates the mucosa and causes coughing which is spasmodic in character because the material is thick and difficult to expel Others believe the paroxysms are due to the toxic effects of the organisms on the central nerv

ous system The tracheobronchial glands are usually enlarged and remain so for a few weeks after the disease is over

Signs and Symptoms The incubation period is from 14 to 28 days Whooping cough may be divided into three phases

Phase 1 The onset is usually insidious with cough accompanied by a catarrhal condition of the upper respiratory tract The fever curve at the start may be of a low type During this phase the patient may have a series of coughing spells which are usually nonproductive These coughing spasms are particularly troublesome during the night and early morning hours The organisms may be found on potato *agar culture plates During the terminal part of this stage* lasting anywhere from one to two weeks the coughing spells increase in severity and the transition to the second phase begins

Phase 2 The paroxysmal stage The second phase lasts approximately two to six weeks During this time a series of coughs accompanied by inspiratory whoops are audible These spasms may be readily provoked by any irritation of the patient An effort syndrome such as fast walking running climbing up or down stairs will precipitate a paroxysm In infants sensorium disturbances will provoke the characteristic whoop These spasms are quite numerous during the day but seem more prolonged during the sleeping hours The irritation set up in the pharynx by the coughing spells may invite edema and considerable stagnant mucoid material In these cases a moist character to the cough is noticed and it is usually terminated with an expulsion of this mucoid material either by expectoration or vomiting Gradually the number of spells during the day and night start to subside and the third phase begins

Phase 3 This is the receding or convalescent stage lasting from two to four weeks Infrequently this stage prolongs itself or has an interim of quiescence and then is repeated long after the expected time for recovery has passed During this period the number of whoops diminishes and the severity is decreased In fact toward the terminal stage of this phase the spasms are only brought about by provoking or irritation or self induction on the part of the patient

Complications The severe paroxysms may invoke an epistaxis or a cerebral accident Occasionally ruptured blood vessels in the conjunctiva over the eye may occur Especially encephalitis has been noted in the height of whooping cough The danger in whooping

cough is the secondary invaders causing a pyogenic pneumonia Bronchopneumonia and atelectasis causing lung collapse occasionally empyema have been mentioned Due to the intense strain in coughing herniations in the abdominal wall may occur

Diagnosis Diagnosis may be difficult during the initial stage though cough plate cultures are helpful An early lymphocytic leukocytosis points to whooping cough Influenza and bronchitis are most often confused with pertussis but can usually be eliminated from diagnosis when all symptoms are considered

Prognosis The mortality rate in children under four varies from 10 to 20 per cent It is higher during the winter months when bronchopneumonia is common and in midsummer when intestinal disturbances are frequent The general rule is—the younger the child the more serious the prognosis If the initial stage is prolonged the paroxysmal phase is not so severe

TREATMENT

The patient should be isolated particularly if there are other young children in the house for a period of three weeks after the whoop begins

1 Bed rest during the catarrhal stage and for a short time during the paroxysmal stage is indicated for children under four years of age This is done to prevent severe complications The patient s head should be elevated with two or more pillows which are equipped with rubber protectors However if the child is afebrile and the attack is mild it may be most convenient to allow him to remain out of bed Plenty of fresh air and natural sunlight are important Care should be taken to see that the patient is warmly dressed out of drafts and properly isolated

2 Proper nutrition should be maintained It may be best to give a child frequent small semisolid feedings rather than three regular meals Glucose or sugar may be added to the diet to combat acidosis from vomiting If vomiting occurs the patient should be fed again about ten minutes after the paroxysm ends Improper feeding may result in persistent vomiting wasting and lowering of resistance

3 If vomiting is severe gastric lavage with sodium bicarbonate 3 1 Gm (46 5 grains) to the pint once or twice daily combined with small rectal or drip saline infusions containing five per cent glucose

is helpful *In these cases plain water sugar water or a small amount* of fruit juice should be given cautiously orally

4 For the poorly nourished patient transfusions of citrated blood, 50 to 150 cc being given according to the age of the patient may be a lifesaving measure Intramuscular injections of whole blood are frequently helpful in quantities of 20 to 30 cc Five per cent glucose solution may also be administered intravenously in 50 to 100 cc amounts

5 Drug treatment is symptomatic and usually a simple expectorant mixture as

℞ Antipyrine	0 533	Gm	(8 gr)
Ammonium chloride	2 66	Gm	(40 gr)
Syr linonis	30	Gm	(1 oz)
Aqua dest q s	60	Gm	(2 oz)

Sig Teaspoonful every three hours

is all that is necessary Other drugs which may be of use are

a Antispasmodics

(1) Belladonna seems to be the drug of choice It is given in increasing doses beginning with 0 2 cc (3 minims) three times a day increasing one minim per dose per day until signs of toxicity appear

(2) Ephedrine 0 008 to 0 016 Gm (⅛ to ¼ grain) two times a day should be used with caution

(3) Other drugs which have been recommended are eumydrine four to ten drops of a 0 1 per cent solution three times a day and benzylbenzoate 0 66 to 4 cc (10 to 60 minims) daily

b Sedatives Much sedation is contraindicated since it usually prevents expectoration of mucus Bromides chloral codeine ether or luminal may be used

(1) Bromides usually the ammonium salt 0 133 Gm (2 grains) with tincture of belladonna 0.2 cc (3 minims) and chloral *hydrate* 0 133 Gm (2 grains) are frequently given

(2) Luminal is probably the drug of choice It is prescribed in tablet or powder form in doses of 0 004 Gm (1/16 grain) for an infant and 0 008 to 0 016 Gm (⅛ to ¼ grain) for older children three or four times a day If vomiting is severe it may be prepared in special ampules for injection

(3) Ether in oil by rectum one part ether to three parts oil may be effective providing severe bronchitis or broncho*pneumonia are* not present

c Expectorants Wine of ipecac 0 133 cc (2 minims) ammonium chloride 0 133 Gm (2 grains) or potassium iodide 0 133 Gm (2 grains) or a combination of the latter two have been recommended

d Vitamin C (ascorbic acid) seems to antagonize the growth of B pertussis and inactivates its toxin It is given in tablet form by mouth in doses of 200 mg daily for the first week 150 mg daily for the second week and 100 mg daily for the third week Half this dose is sufficient for children under one year of age

6 *Specific Treatment*

a Vaccines In general vaccines during the acute infection seem to be of little value In most cases children are not ill enough to warrant this procedure If treatment can be started early in the catarrhal stage before the paroxysms develop antigen 0 2 cc may be given as the initial dose to an infant increasing the amount 0 2 cc. daily up to 1 0 cc providing no reaction occurs

b Sera Hyperimmune serum has proved itself most beneficial in the treatment of sharp cases of whooping cough

c Chemotherapy While the sulfonamides have no direct effect on whooping cough most complications of the disease respond very well to the drugs

d Other measures

(1) The severity of the cough may be relieved by one or two x ray exposures of one-quarter to three-quarters of a pastille dose applied to the back through a suitable filter

(2) Inhalations of seven per cent carbon dioxide in air or oxygen or a mixture of helium and oxygen may have a good effect

7 *Prevention* Vaccine injections have been followed by good results Usually 8 cc of vaccine are used each cubic centimeter containing ten billion killed organisms It is given in increasing amounts at weekly intervals for three weeks the first dose being 1 cc. in each arm and 1 5 cc in each arm on the other two visits

SMALLPOX (VARIOLA)

Smallpox is an acute communicable disease characterized by a prodromal period of three to five days followed by an eruption and uniform stages of evolution

Etiology The disease occurs throughout the world especially during the winter months People of all ages are attacked but it is most serious and fatal in young children Infants before and after birth are susceptible Negroes are affected more often than white people and the disease is more severe and fatal in the colored group

The cause of the disease is a filterable virus but the specific agent is not certain Guarnieri described certain inclusion bodies found in

the cells which he called *Cytoryctes variolae* A protozoan or bacterial etiology has also been suggested The virus can be demonstrated in the fluid of the lesions in the lesions and the crusts

Smallpox is transmitted directly in most cases particularly by the droplet method However, contact with the patient scabs scales or fluid from the lesions is a common means of communication Whether the disease is air borne is a question though it is probable that any virus disease may be transmitted in this way for a very short distance

Pathology The most extensive changes are found in the skin and mucous membranes since the eruption affects both The lesions complete the evolution of a macular papular vesicular and pustular phase and terminate with crust formation In the pustular stage umbilication occurs When the lesions heal a central pit or depression remains extending into the corium of the skin The severity of the depression will propose the terminal cicatricial changes and may result in pit marks The parenchymal organs present cloudy swelling and occasionally focal necrosis A lymphoidal hyperplasia takes place throughout the body

Signs and Symptoms The incubation period may be from 10 to 18 days but is usually 12 days The prodromal period of three to five days usually presents the picture simulating an influenzal infection Chills insomnia headache myositis are the commonest symptoms The myositis may be quite intense and exaggerated as a low back pain Usually recovery after this period is followed by the presentation of the eruptive stage The eruptions are centrifugal in distribution occurring first on the face and then on the extremities A paucity of eruption is usually noted on the torso proper The eruptions pass through a transition of macular papular rapid vesicular to pustular stages taking approximately seven to nine days to reach the height of their evolution The lesions are usually quite discrete with a halo about them Approximately seven to nine days of desiccation and terminal crustation occur before the completion of the course of the disease Fever is quite characteristic of the prodromal period and a secondary rise occurs during the height of the pustular period

Complications Secondary infection may cause a streptococcemia abscesses furunculosis areas of gangrene and erysipelas Pneumonia and encephalitis are not uncommon sequelae

Diagnosis Chickenpox may be readily differentiated by the erup

tion occurring in the febrile stage and the centripetal distribution of the lesions pustular syphilis by its history chronicity and serological examination Other skin diseases, as measles rubella lichen urti catus dermatitis venenata and medicamentosa erythema multiforme scabies pityriasis and impetigo have their characteristic history and findings

Prognosis Prognosis in smallpox varies in different epidemics and death usually due to overwhelming toxemia may range from 20 to 50 per cent

TREATMENT

Vaccination and re vaccination are fool proof measures in eradi cating smallpox Emergency vaccinations may be done with intra dermal chorioallantoic chick embryo vaccine Otherwise vaccination should be done within one year after birth repeated at the pubescent and again at the adolescent stages of life

Specific immuno transfusions colloidal gold and chemotherapy have been found wanting after the disease has occurred Symptomatic care is indicated The patient should be isolated and quarantined Vaccination of all contacts should be rigidly enforced It is prefer able that the patient be moved to an isolation hospital for care with subsequent fumigation and cleansing of his living quarters The patient must be kept under strict quarantine until all crusts have separated particularly those on the palms of the hands and soles of the feet

The symptomatic care may be outlined as follows

1 Rest in bed with plenty of fresh air

2 The diet during the febrile stage should be limited to liquids as milk buttermilk eggnogs and broths After the initial fever nourishing solid food as meat eggs and the more easily digested vegetables should be given in preparation for the stage of suppura tion During the secondary fever diet is again limited to liquids

3 Joint pains may be relieved by hot fomentations

4 The patient should receive plenty of water and fruit juices

5 Headache which is one of the common complaints of these patients should be treated by the administration of phenacetin 0 33 Gm (5 grains) three or four times a day or acetylsalicylic acid 0 66 Gm (10 grains) three times a day and occasionally codeine sulfate 0 033 to 0 066 Gm (½ to 1 grain) as needed

6 Tepid sponges cold packs or sponge baths are efficacious in the febrile states Weak potassium permanganate tub soakings are soothing and will alleviate most subjective complaints

7 Delirium is treated by the use of sedatives such as chloral hydrate 1 to 2 Gm (15 to 30 grains) per rectum or morphine sulfate 0 033 Gm (½ grain) subcutaneously

8 Conjunctivitis requires irrigation of eyes three to four times daily using normal saline solution or boric acid solution and anointing the lids at night with an ointment of yellow oxide of mercury 0 033 to 30 Gm (½ grain to 1 oz)

9 Annoying throat conditions may be alleviated by the use of cooling drinks The mouth should be kept clean by frequent washings potassium permanganate solution 1 4000 is probably most effective If inflammation of the tongue is severe it usually yields to painting with glycerite of tannic acid but incision may sometimes be required

10 Morphine 0 011 Gm (⅙ grain) hypodermically is probably the most certain medication for relief of pain which is sometimes extremely severe Acetylsalicylic acid 1 Gm (15 grains) three times a day is very effective in some cases

11 The crusts should not be removed but should be permitted to be soaked off or ointments as bicarbonate of soda 8 Gm (2 drams) and petrolatum 30 cc (1 oz) applied during the terminal stages

DIPHTHERIA

Diphtheria is an acute communicable disease usually characterized by involvement of the mucous membranes of the respiratory tract or system with the production of a pseudomembrane and symptoms due to toxemia

Etiology Diphtheria is commonest in children under the age of ten during the late fall and winter months It occurs the world over and is usually endemic in large cities but often becomes epidemic

The disease is caused by the Klebs Loeffler bacillus which does not penetrate the mucosa The organism grows best on Loeffler s medium and is identified on staining with Loeffler s methylene blue Other media which identify the organisms more rapidly are impregnated swab sticks with either sterile horse serum or a potassium tellurite medium

Diphtheria is most often transmitted by carriers through active or convalescent cases these being the most positive sources The mode of spread is through the air or by direct contact *via* the droplet method or from freshly soiled articles Epidemics have been caused by contaminated food and milk The portal of entry is through the nose throat or other mucous membrane or by direct inocula tion through open wounds The economic status is considered an important factor in the incidence and lack of proper food poor heating and overcrowded living conditions play their part Susceptibility to the disease varies infants up to six to nine months rarely contract diphtheria and many healthy adults have the organism in their throats without having the disease

Pathology The organism usually remains at the point of focal infection and is rarely recovered from the blood stream The or ganisms Klebs Loeffler bacilli proliferate readily within the selec tive tissue infected liberating a toxin which is absorbed and distrib uted by way of the blood and lymphatic systems The by products of the organism the toxoid toxin and toxon affect first the local tissue and subsequently the parenchymal organs These organs are all involved in diphtheria but the most marked changes of a fatty degeneration occur in the musculature of the heart This fatty de generation displaces the normal cellular arrangements with a terminal edema and interstitial fibrosis Fatty degeneration may also occur in the central and peripheral nervous system

Signs and Symptoms The incubation period is from two to seven days The commonest site of involvement is the nasopharynx The onset is insidious with a complaint of general malaise slight fever and difficulty in swallowing Anatomically the portals of en trance might be divided into nasopharyngeal mesopharyngeal laryn geal or involvement of all of the passages in the upper respiratory system The mesopharynx is the most commonly involved At the onset a thin film may occur over the tonsils assuming later a more gelatinous appearance being white or gray in color The depth of the color change in the pseudomembrane is subject to the enmeshing of polymorphonuclear leukocytes fibrin deposits organisms and erythrocytes The membrane may progress upward forward and/or downward resulting in the clinical types noted Throughout the period absorption of toxins occurs Occasionally a symbiotic infec

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11 The crusts should not be removed but should be permitted to be soaked off or ointments as bicarbonate of soda 8 Gm (2 drams) and petrolatum 30 cc (1 oz) applied during the terminal stages

DIPHTHERIA

Diphtheria is an acute communicable disease usually characterized by involvement of the mucous membranes of the respiratory tract or system with the production of a pseudomembrane and symptoms due to toxemia

Etiology Diphtheria is commonest in children under the age of ten during the late fall and winter months It occurs the world over and is usually endemic in large cities but often becomes epidemic

The disease is caused by the Klebs Loeffler bacillus which does not penetrate the mucosa The organism grows best on Loeffler s medium and is identified on staining with Loeffler s methylene blue Other media which identify the organisms more rapidly are impregnated swab sticks with either sterile horse serum or a potassium tellurite medium

TREATMENT

1 Prophylaxis The disease may be placed in the same category as that of variola i e extinction by active immunization Subsequent susceptibility should be determined by the Schick test and if positive a repetition of the course of immunization should be carried out at once

2 Active Treatment Isolation should be enforced quarantine is not essential Specific antitoxin should be administered intramuscularly in large doses—20 000 to 60 000 units as early as possible Cultures must always be taken but regardless of the culture report if a case clinically suggests this disease antitoxin must be given If the patient is susceptible to the foreign protein of the serum serum tolerance should be induced prior to the giving of the large doses required for the disease

3 Absolute rest should be recommended in every case for a minimum of four weeks and gradual rehabilitation allowed to take place

4 During the acute stage a liquid diet is preferable and should contain adequate carbohydrates sufficient vitamins especially B and C and a minimum of proteins Overfeeding should be avoided in order to prevent vomiting Difficulty in feeding which may arise owing to paralysis of pharyngeal muscles can be overcome by feeding through a nasal catheter After the acute stage is passed the diet may be increased to include stewed fruits soft boiled eggs gelatin light puddings gruel and well-cooked cereals

5 For relief of the dyspnea turpentine stupes applied to the neck and upper chest have proved of benefit As an emergency measure it is beneficial to rub the chest with camphorated oil followed by application of hot flannels

6 If evidence of cardiac involvement is noted ten per cent glucose in daily doses of 250 to 500 cc should be administered intravenously in all cases Morphine sulfate 0 004 to 0 006 Gm (1/16 to 1/10 grain) is administered subcutaneously as needed to secure rest and quiet The cardiac stimulants are of little value but caffeine sodium benzoate 0 133 to 0 33 Gm (2 to 5 grains) subcutaneously is of value in vasomotor collapse No drastic catharsis no bathroom privileges and no large meals are to be given during convalescence and with cardiac involvement the period of absolute bed rest is increased

tion (usually streptococcic in origin) occurs with the Klebs Loeffler bacillus and results in a marked involvement of the area affected and a severe lymphadenitis This lymphadenitis is termed a bull neck The size of the pseudomembrane does not determine the severity of the toxemia

Complications Early myocardial changes are most important in the morbidity mortality rate of this disease Evidence of a tachy cardia bradycardia syncope, nausea and vomiting and hypertension are usually related to the myocardial damage Palatinal paralysis ocular disturbances (ciliary muscle), peripheral neuritis and absence of knee jerks are evidences of central nervous system involvement Pneumonia and respiratory paralysis are of a serious character The difficulty in respiration due to atresia or partial stenosis of the larynx *is most significant There is a mechanical obstruction due to* the existence of and extension of the membrane into the trachea and bronchi It may cause suffocation and a fatigue syndrome

Diagnosis Follicular tonsillitis has a sudden onset high fever severe pain in the throat and hard glands and is self limited within approximately 72 hours Acute streptococcic anginas are character ized by marked hyperemia over the mesopharynx with positive cultures to support the diagnosis Vincent s angina is insidious in onset of an ulceromembranous character and has evidence of alve olar or oral sepsis Positive smears verify the diagnosis Scarlet fever is characterized by the triad of a sore throat glossitis and punctiform rash Syphilitic angina is chronic and supported by a history and positive serological reaction Laryngeal diphtheria must be differ entiated from foreign bodies acute catarrhal laryngitis (croup) retropharyngeal abscess laryngismus stridulus enlarged thymus con genitally relaxed larynx *and diverticulum*

Prognosis The prognosis is directly related to the day of onset of the disease and the rapidity or latency of the treatment with the specific antitoxin The severity of the complications without proper management quite often cause an exitus Rarely is the disease self limited with a recovery independent of specific treatment The com plications infrequently leave residual damages especially to the nervous system

dence of encephalomeningitis During the course of convalescence chill marked pyrexia and pain in the scrotum are evidence of an epididymoorchitis The possibility of sterility makes this a serious complication Oophoritis expressed in terms of extreme pain in either lower quadrant or bilaterally in the female may also result in sterility

Diagnosis The disease must be distinguished from

1 Anaphylactic reactions due to neurogenic factors

2 Infections *i e* tuberculosis undulant fever tularemia syphilis and pneumonia

3 Von Mikulicz s disease ruled out by blood smears ordinary cervical lymphadenitis and suppurative parotitis following dental caries or trauma

4 Tumefactions usually of long standing of a benign or malignant character

5 Foreign bodies inspissated mucous plugs cicatrices and calculi

6 Emphysema as occurring in musicians or children blowing air into the ducts usually transient in character

Prognosis Mumps even occurring with complications is never fatal and the outcome is an early return to health

TREATMENT

Mumps is a reportable and placardable disease The treatment is particularly symptomatic but where complications are suspected 20 to 60 cc of convalescent mumps serum has proved of value Relief of pain is most frequently brought about by warm applications dry or moist to the glands involved Bed rest is essential for these cases to prevent complications Adults particularly must be told about the potential complications and warned to avoid overactivity

Occasionally when glandular swelling is at its height and the patient is restless and uncomfortable with a moderately high fever phenacetin 0 2 Gm (3 grains) and caffeine citrate 0 033 Gm (½ grain) administered in a capsule and repeated in three hours will be found useful as an emergency remedy

SCARLET FEVER (SCARLATINA)

Scarlet fever is an acute communicable disease usually characterized by a sore throat glossitis and a punctiform rash

7 In severe laryngeal involvement intubation or tracheotomy must be resorted to

MUMPS (EPIDEMIC PAROTITIS)

Mumps is an acute communicable disease characterized by an inflammation of the salivary glands most commonly of the parotid

Etiology The disease is caused by a filterable virus which has been recovered from the saliva and also from the blood of infected individuals The portal of entry is most commonly through the mouth by the droplet method though articles contaminated by saliva or air borne infection must be considered

Pathology The involved glands are red swollen and moist Mononuclear infiltration occurs around the blood vessels and the ducts The latter may be dilated and obstructed with retained saliva The adjacent lymph nodes are swollen and congested but suppuration of the glands rarely if ever occurs

Signs and Symptoms The incubation period is from 14 to 21 days The onset is usually insidious though in some instances it may be quite acute It is characterized by chills and fever the latter more frequently exaggerated than a low curve Pain on the side involved is noted as a subjective complaint with difficulty in mastication and deglutition Objectively the mucous membranes of the mouth and pharynx are slightly injected and edematous Edema may be noted about Steno s duct Observable swelling occurs between the ascending ramus of the mandible and the mastoid process It usually assumes a grotesque appearance The opposite side may become involved about two or three days after the initial infection has been noticed The swelling approaches its highest stage in three to five days and a similar amount of time elapses before the swelling subsides Palpation elicits pain over the swollen gland and a rather doughy elastic character to the skin Infrequently the submaxillary or sublingual glands may be involved

Complications Complications occur most frequently in patients beyond the pubescent years and hence are more serious in nature Mastodynia or mastitis is complained of Gastrointestinal upset and jaundice with intense pain in the epigastrium are evidence of hepatitis or pancreatitis Occasionally convulsion stupor and neck rigidity with a spinal fluid finding of a high lymphocytic cell count are evi

vary from pale pink to deep scarlet and disappears on pressure leaving a white mark on a background of scarlet The skin is hot and dry and may be edematous The face is usually flushed without rash except for the area around the mouth which remains white There is a leukocytosis of from 10 000 to 18 000 and a trace of albumin is found in the urine

As the fever increases the throat symptoms become more severe the fever usually reaches its height in 24 hours remains there for four or five days and then gradually falls by lysis as the rash fades Desquamation begins about the sixth day when the temperature falls and eruption disappears The type of desquamation depends on the texture of the skin It may peel off in tiny powdery scales from parts of the body where the skin is sensitive while tough flakes or even slabs may come off the palms of the hands and soles of the feet Desquamation does not always occur especially not in patients treated early with scarlet fever antitoxin or convalescent serum

In the septic type a profuse nasal discharge is present almost from onset Throat symptoms are very severe and there may be difficulty in swallowing Cervical adenopathy may be marked with extensive brawny induration of the neck occasionally Patches on the tonsils and throat suggest diphtheria Despite the unfavorable appearance of the patient prognosis is much more hopeful than in the toxic cases The fever reaches an unusual height of 40 to 41 1° C (104 to 106 F) in the latter the pulse is rapid as are the respirations and the patient may be irrational Death often occurs before the rash appears

Complications The complications of scarlet fever may result from the bacterial invasion or they may be due to the erythrogenic toxin The bacterial invasion may cause peritonsillar abscess sinusitis otitis media and mastoiditis Rarely bacteremia results in endocarditis and onychias and paronychias of the fingers and toes The toxin may cause lymphadenitis perleche arthritis synovitis and nephritis

Diagnosis Measles can be readily differentiated from scarlet fever by its upper respiratory infection with its rash occurring on the face and body The rash is of a maculopapular character Rubella has a postcervical adenitis and a rash much larger in size than the scarlatiniform rash which is present on the face and body Exanthem subitum has two or three days of high fever followed by a transitory

Etiology Scarlet fever is caused by a variety of strains of Hemolytic streptococci It is generally spread by direct contact especially through throat nasal and ear secretions it may also be communicated by clothing toys and other articles by a third person or through infected milk As in diphtheria the portal of entry is through the respiratory passages Localization of the primary infection is most frequently in the throat or nasopharynx, but the organism may enter the body at other sites and in these cases the local symptoms in the throat and nasopharynx are often mild The total number of cases in a community seems dependent on the size of the population probably because in large cities there are more carriers An individual usually becomes immune after an attack of scarlet fever but some people experience recurrences which may be explained by the fact that so many strains of the Hemolytic streptococci cause the disease

Pathology The rash is due to an erythrogenic toxin causing a vascular irritation The toxemia causes cloudy swelling in the parenchymal organs as in most acute infectious diseases In the septic cases there is an accompanying bacteremia and resistant foci of infection in the parenchymal organs In the heart the commonest lesion causes a focal accumulation of cells *i e*, mostly lymphocytes, histiocytes and plasma cells Histologically similar lesions occur in the kidneys The degree of tissue reaction is most severe in those cases that die after the tenth day The reactions are most conspicuous in patients with bacteremia

Signs and Symptoms The incubation period is from two to seven days The onset is usually sudden with a complaint of sore throat nausea and vomiting headache and fever The throat shows evidence of marked injection and edema Occasionally exudate is present on the tonsils The tongue will be coated at the start and subsequently desiccates from the tip backward presenting a red appearance on the fourth day with the red glistening papillae present This has been spoken of as the raspberry tongue of scarlet fever but is best termed the glossitis of the disease

The rash appears from 10 to 36 hours after the onset of symptoms It is a densely scattered erythematous punctate rash which may appear confluent It is noted first on the upper chest and back and then rapidly spreads over the body and extremities The color may

h All surgical and medical complications are to be treated symptomatically In the event of a bacteremia meningitis or inaccessible surgical point chemotherapy is to supplement specific therapy

3 Specific Treatment

a Dick antitoxin of 300 000 neutralizing doses is recommended in sharp cases of scarlet fever

b Human convalescent scarlet fever serum is preferable because no allergic reaction occurs If available human convalescent serum may be given in 20 to 80 cc doses intravenously with no untoward reaction The therapeutic value may be noted within 24 hours after usage

4 Miscellaneous Scarlet fever is a reportable and quarantinable disease The average period of quarantine is from three to six weeks

infantum eruption In erythema infectiosum (fifth disease) there is a marked morbilliform rash on the face and extremities with extremely marked pyrexia The rash of scarlet fever can be proved in differentiation from the scarlatiniform erythema with the Schultz Charlton test Human convalescent serum may be used intradermally in verifying the blanching test

Prognosis Prognosis in scarlet fever is dependent upon the virulence of the infection individual resistance and the presence and type of complications In epidemics mortality may be as high as from 15 to 40 per cent while at other times only 0 1 per cent of patients may die

TREATMENT

1 Prophylaxis A Dick test will reveal susceptibility to scarlet fever Active immunization with the Dick toxin is recommended to develop immunity Although prolonged in its treatment investigative evidence shows that intracutaneous injections of 750, 3000 and 11 000 skin test doses at two week intervals give very satisfactory results

2 General Treatment

a Rest in bed is imperative throughout the acute stage of the disease and until complications if present disappear Usually children should be kept in bed for about 18 days and adults for two weeks

b Adequate amounts of fluid should be given in mild cases the patients can usually take enough by mouth

c Diet should be fluid and nutritious during the first week if the throat is intensely inflamed followed by a soft or full diet In general the diet does not have much influence on the outcome of the disease

d Gargles are not usually indicated An antiseptic mouth wash if properly used may be employed but it is not advocated for small children

e Cold applications in cervical adenitis are of value

f For the toxic conditions with marked cyanosis caffeine sodium benzoate 0 2 to 0 33 Gm (3 to 5 grains) in frequently repeated doses is of some value

g When mild nephritis develops the patient should be kept in bed on a low protein salt free diet The indication for immediate treatment is the development of uremia Removal of blood (250 cc in five year old children 300 cc in ten year-old children and 500 cc in adults) followed by an equal injection of physiological saline solution usually brings the patient out of a state of coma and relieves the convulsions At times it may be necessary to repeat this treatment

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CHAPTER XIX

Acute Infections

(Continued)

MEASLES

Measles is an acute communicable disease characterized by an upper respiratory infection with an exanthem and an enanthem

Etiology Measles is caused by a filterable virus which enters the system through the nasopharynx It is one of the most readily trans missible of exanthemata being particularly of an air borne character The period of incubation is from 10 to 18 days most commonly 14 days

Pathology The pathological changes are primarily confined to the mucous membranes and skin The mucous membranes of the nasopharynx and nasopharyngeal tract and infrequently the gastro intestinal tract are inflamed and a cellulitis is noted

Signs and Symptoms The onset is usually ushered in by cough fever and nasopharyngeal effusion The catarrhal phenomena are a progressive upward and downward involvement of the mucous mem brane resulting in conjunctivitis with epiphora photophobia and a laryngotracheobronchial irritation This prodromal period may last from three to seven days during which time an enanthem is present in the mesopharynx and Koplik spots are noted on the oral mucous membrane Following the prodromal period a slight drop in tem perature may be noted succeeded by a maculopapular eruption begin ning on the face This polymorphous crescentic eruption progresses downward over the neck body and extremities It assumes a bright red color and reaches its height in three to five days taking an equal amount of time to recede This eruption may be discrete or confluent and rarely is of a hemorrhagic type Occasionally desquamation may be noted at the point of eruption

Complications Aural sepsis occurs most frequently followed by adenitis Otitis media occurs in 17 per cent of cases and broncho pneumonia in 13½ per cent Encephalitis and encephalomyelitis have been recognized as sequelae to the disease

Diagnosis Measles may be confused with rubella The latter has its characteristic postcervical adenopathy and the lesions are smaller and transient in their appearance Scarlet fever presents its characteristic triad of sore throat glossitis and pin point rash Serum sickness usually has a positive history of a toxo-allergen There is invariably the angioneurotic edema and accompanying pruritus The rose spots of typhoid fever appear on the trunk and abdomen and the Widal test is quite conclusive

Prognosis Measles is important because of its so called status morbillosus The serious age group is between two and five years Deaths are usually due to the acute pulmonary edema in the eruptive stage or to the complicating sepsis and encephalitis during convalescence

TREATMENT

1 **Prophylaxis** Prevention should not be considered in that only passive immunity may result and subsequent exposure will again require the same measures as on the initial attempt to prevent this disease Modification is the desired procedure especially if the individual has recently convalesced from serious illness or operation Modification may be brought about by whole blood injections from serologically negative individuals (usually parental blood) Convalescent measles serum has a high opsonification index and is preferable it is given in 10 to 20 cc doses intramuscularly Normal serum may also be used as well as immune globulin The latter a placental extract should be given early in the incubation period If given late little effect is noted

2 **Isolation** Measles is a reportable and placardable disease Therefore all patients should be placed under isolation as required by most state laws for a period of 14 days

3 **General Treatment** There is no specific serum for the treatment of measles The sulfonamides have not been successful in virus infections Rest in bed hydrotherapy internal and external no catharsis and symptomatic control of the cardinal symptoms are indicated

The eyes may be protected from strong light and should be bathed frequently with physiological saline or boric acid solution and the eyelids should be kept free from crust formation by anointing them with petrolatum

TREATMENT

German measles is a reportable and placardable disease but is considered the mildest of all contagious illnesses The treatment is particularly symptomatic and is of interest chiefly in its differentiation from the other communicable diseases

The skin may be protected by anointing daily with carbolized petrolatum (carbolic acid 0 33 cc — 5 minims — to petrolatum 30 cc — 1 ounce) or oil of eucalyptus and olive oil equal parts of each

During the three or four days of active symptoms in this disease quinine sulfate 0 133 or 0 2 Gm (2 or 3 grains) to a teaspoonful of chocolate syrup may be used

ERYSIPELAS

Erysipelas is a self limited acute erythematous inflammation of the skin caused by the *Streptococcus haemolyticus* and accompanied by a severe constitutional reaction The lesion is characteristically a red swollen area with sharply demarcated and elevated border with small flamelike pseudopodia extending beyond the border

Etiology The causative organism is a hemolytic streptococcus of no constant strain The organism enters the skin at the site of a wound fissure or abrasion Often there is no recognizable channel Erysipelas is commoner in women than men and occurs most frequently in individuals between the ages of 35 and 55 years but does occur in early infancy and old age Persons who have recently undergone an operation and women in the puerperium are the most frequent victims of the disease Undernourished and debilitated individuals are also more susceptible The disease occurs in every part of the world but is usually more frequent and more severe in temperate climates

Pathology Sections through the infected area show marked congestion of the capillaries edema areas of skin necrosis and lymph spaces crowded with streptococci The distribution of the streptococci is peculiar for they are found exclusively in the lymphatic vessels in greatest numbers at the margins of the inflamed areas they are absent in the central portion and are seldom found in the contents of the blebs Leukocytes are found scattered throughout the area and mononuclear cells are present in great numbers in the corium and lymphatics A powerful toxin is produced by the organ

Frequent instillations of albolene into the nose relieve the discomfort from rhinitis

Oral hygiene should be particularly noted and early treatment of the *perleche* should be carried out Severe laryngitis or distressing cough may be ameliorated by steam inhalations with menthol or compound tincture of benzoin added

Cough may be controlled with small doses of codeine 0 004 to 0 016 Gm (1/16 to 1/4 grain) hypodermically

Alcohol sponges or tepid baths may be used to lower the temperature and quiet the patient

The indications for sulfonamides are in the event of any evidence of secondary infections of the streptococcus and other bacteria that respond to this therapy

GERMAN MEASLES (RUBELLA)

German measles is an acute communicable disease characterized by a postcervical adenitis and a fine maculopapular rash

Etiology The causative agent of rubella is a virus It occurs in greatest numbers in the second and third decade of life because it assumes an epidemic proportion in from five to ten year periods The disease leaves a lifelong immunity

Signs and Symptoms The disease may be ushered in with a moderate upper respiratory disturbance These mild catarrhal symptoms are accompanied by a low grade fever curve The individual is usually cognizant of a lymphadenitis located in the postauricular postcervical and occipital regions These glands are small tender and readily palpable The rash occurs on the face and has a mottled appearance and subsequently is noted on the body in the form of a discrete reddish orange color slightly larger than the punctiform rash of scarlet fever but smaller than the morbilliform rash of measles The rash lasts from 12 to 48 hours at the longest The glandular involvement persists from two to ten days after the rash has disappeared and is quite characteristic of the disease

Complications Complications are rarely encountered A few cases of encephalitis have been reported but there is a question as to the number

Prognosis Fatalities have not been reported except as the result of concurrent infections or when the rubella was a coincidental communicable disease superimposed upon some severe infection

otitis media mastoiditis pericarditis endocarditis empyema and arthritis

Diagnosis The diagnosis can usually be made at a glance In the acute staphylococcal infections the skin feels harder the margins are not definitely demarcated and the lesion spreads more slowly The systemic symptoms are lacking The method of spread and the absence of constitutional symptoms differentiate acute eczema and the allergic dermatitides

Prognosis In the very young or in the aged most patients die although females have a better chance of survival than males at all ages Prognosis is guarded in individuals having chronic diseases especially of the kidneys

TREATMENT

1 Isolate the patient

2 Fluids up to 4000 cc daily should be administered

3 A high caloric and high vitamin (particularly A and D) diet should be given

4 Codeine sulfate 0 033 Gm (½ grain) and acetphenetidin 0 2 Gm (3 grains) every four hours are usually sufficient to allay pain and induce sleep

5 The bowels should be regulated an enema may be given every other day and a mild laxative as mineral oil 30 cc (1 ounce) daily

6 Hot or cold compresses may give comfort

7 Abscesses should be incised

8 Sulfadiazine is effective and is the drug of choice The initial dose is 4 Gm (60 grains) with an equal amount of sodium bicarbonate Then 1 Gm (15 grains) is given every four hours with sodium bicarbonate in equal amount until the optimal blood level is reached The drug may then be reduced to 1 Gm (15 grains) four times a day and should be continued until the temperature has been normal for 24 hours

9 Multiple small transfusions 50 to 100 cc should be given in severe toxemia

10 Antiserum and antitoxin may be administered

11 X ray and ultraviolet therapy have been advantageous in some instances

isms and the viscera undergo changes which are common to acute infections i e, cloudy swelling and splenomegaly

Signs and Symptoms The incubation period is about three days but varies from two to eight The onset is sudden with a rise of temperature malaise headache sometimes vomiting and not infrequently delirium

Local Reaction The local lesion begins most often on the face especially about the nostril or the inner canthus of the eye The first sign may be a red area extending from the nostril or the inner canthus of the eye across the bridge of the nose The area is hard, tense shiny and tender with a well defined edge which is usually irregular and bright red The process spreads rapidly the marginal areas retaining the features noted but the center tends to fade Small red pseudopodia may be seen at the periphery marking the extension of the process in the lymphatics Extension is always by continuity Small vesicles or blebs may appear Desquamation of a flaky type occurs as the process fades out Great alteration appears in the facial features as the process extends rapidly on the cheek and over the bridge of the nose to the opposite side giving the butterfly appearance The eyelids become markedly swollen red and glistening and the eyes cannot be opened there is rarely involvement of the cornea The lesion seems to stop at the hair line and at the ramus of the jaw However occasionally it extends down the neck and over the chest The regional lymph nodes are involved and enlarged

Systemic Reaction The fever is high early in the course of the disease and rises to 38 3 to 40° C (101 to 104 F) A feeling of weariness anorexia slight headache and chilly sensations increase quickly The face is flushed and the eyes are bright The skin is hot and dry with periods of drenching sweat the tongue is coated and the lips are parched

The blood usually shows a leukocytosis of 12 000 to 20 000 with an increased percentage of polymorphonuclear leukocytes The spleen is seldom palpable The urine shows a febrile albuminuria and often contains urobilin Relapses and recrudescences occur

Complications Abscess of the eyelids postauricular preauricular and cervical lymph glands and acute sinusitis are frequent Pharyngeal abscess may also occur Gangrene of the skin is a rare sequel Pneumonia may be a terminal event Among the complications are

the long axis of the bowel The spleen is usually enlarged Cloudy swelling of the liver and small areas of focal necrosis are seen Bronchitis is commonly present and there may be pneumonia The myocardium becomes flabby The kidneys show cloudy swelling

Signs and Symptoms The incubation period is from 7 to 14 days Usually there are no symptoms during this time though there may be a slight fever at night The onset is slow the most prevalent early symptoms being headache epistaxis and a general feeling of weakness which is not serious enough to necessitate neglect of the patient s work As time goes on the malaise becomes more pronounced the temperature begins to rise the appetite is poor and the body aches The picture is one of mild progressively increasing intoxication During the first week of the disease the temperature continues to rise until it attains a height of 39 to 40 5 C (102 to 105 F) the pulse rate is increased but not in proportion to the degree of fever At the end of the first week a mild degree of bronchitis enlargement of the spleen bradycardia leukopenia and the characteristic rose spots are present The latter are small pink macules which disappear on pressure they usually appear in crops and while they are most often found over the abdomen and lumbar region they may be noted on other parts of the body They are probably due to dilatation of the capillaries and small quantities of typhoid bacilli are often found on section The urine is of a dark color with high specific gravity albumin and a few casts The patient is weak pale and looks sick with the onset of diarrhea and related symptoms a state of exhaustion prevails

Manifestations become progressively worse during the second week the patient is often delirious and may die during this stage During the third week the symptoms become more profound the heart is rapid and weak the lungs are congested the abdomen distended and it is during this period that perforation and hemorrhage may occur In almost all cases of typhoid fever the stools of the patient contain blood after the first week At this time death may occur from intestinal hemorrhage epistaxis or pneumonia or in cases which are not very severe recovery may begin by lysis In the latter cases the temperature gradually returns to normal and other symptoms disappear During this period there may be a relapse which is usually mild though it may be severe enough to cause death

TYPHOID FEVER

Typhoid fever is an acute specific infectious communicable disease caused by the Bacillus typhosus and characterized by blood stream invasion high and continued fever slow pulse, enlarged spleen rose colored rash and diarrhea It is a disease of insidious onset which runs a prolonged course of about 21 days usually ending by lysis

Etiology Typhoid fever is essentially a disease of youth and early adult life generally occurring between the ages of 15 and 25 years Rarely is it seen in infancy or in patients past 50 years of age It occurs in both sexes and is most prevalent during the summer and early autumn months While it has worldwide distribution its incidence has decreased in recent years owing to the improvement of sanitary conditions and prophylactic immunization In general the main sources of the disease are contaminated water ice or milk and infected food Soil contaminated by defective drains and the like may pollute the water and at the same time vegetables from this soil which are eaten uncooked may cause the disease Often the disease is contracted while individuals are on their vacations and have access to milk or water which is not pure Swimming in polluted streams may cause typhoid fever Other causes include typhoid carriers contact with soiled linen or the stools of typhoid patients and consumption of food contaminated by flies or shellfish from infected water People may be exposed to the disease but remain immune to it Usually an attack of the disease results in immunity in those cases where a second attack occurs another strain of typhoid organism or a massive dose of the same organism which caused the previous attack is the cause

Pathology The bacteria enter the body through the gastrointestinal tract from the ingestion of contaminated food or water It is possible that many of these bacteria are destroyed in the stomach but at the same time it must be said that ulcers of the mucosa and submucosa of the stomach and esophagus are frequently found The lymphoid tissues of Peyer s patches and the solitary lymph follicles are most commonly invaded by the bacteria The lymphoid tissue of the lower part of the ileum is inflamed Catarrh throughout the bowel is the commonest finding The long axis of the ulcers parallels

the long axis of the bowel The spleen is usually enlarged Cloudy swelling of the liver and small areas of focal necrosis are seen Bronchitis is commonly present and there may be pneumonia The myocardium becomes flabby The kidneys show cloudy swelling

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Complications The commonest complications are perforation and hemorrhage and these may cause death Perforation is due to rupture of a necrotic Peyer s patch which in turn is caused by a distended bowel or peristalsis The typical picture of shock is evident when perforation occurs Hemorrhage may occur from the nose or bowel and is the result of rupture or necrosis of a blood vessel in a necrotic area While occult blood may be found in the stools of many typhoid patients such slow bleeding is not serious Severe hemorrhage is evidenced by chills marked pallor rapid pulse and absence of abdominal pain the patient lies very quietly and may show evidence of air hunger Other complications include bronchitis and pneumonia thrombosis acute nephritis, cardiac failure neuritis and cholecystitis

Diagnosis Since typhoid fever is so infrequently seen diagnosis may cause some difficulty Formerly diagnosis was made from clinical evidence but now laboratory methods aid somewhat The typhoid organism can be isolated from the blood during the first week of the disease and it may be found in the urine and feces thereafter Blood agglutination by the Widal test indicates the presence of typhoid antibodies Agglutination with a dilution of the patient s serum in a strength of 1 50 or 1 100 is considered positive The value of this test has been somewhat diminished since the advent of prophylactic injections of typhoid vaccine

Diseases which may simulate typhoid fever include malaria miliary tuberculosis subacute bacterial endocarditis typhus fever trichinosis and undulant fever The marked daily variation in temperature in malaria should help in diagnosis as well as examination of blood smears In miliary tuberculosis the pulse temperature ratio is lacking a family history of tuberculosis is usually present, and chest plates blood studies and stool cultures may help in differentiation In bacterial endocarditis the fever is seldom as severe nor as continuous chills are more frequent petechiae appear in the conjunctivae and the presence of dyspnea heart murmurs joint pains and red cells in the urine point to this diagnosis A positive Weil Felix reaction numerous skin lesions and an abrupt onset aid in the diagnosis of typhus fever In trichinosis there is leukocytosis eosinophilia and muscular tenderness

Prognosis Mortality averages from about 6 to 20 per cent or

higher However this comparatively high rate may be explained by the fact that the disease is not frequently encountered and one or two deaths in a year when there are few cases increases the mortality rate The febrile period usually ends at the beginning of the fifth week though it may continue for more than six weeks The duration of this period has little effect on the mortality

TREATMENT

1 Absolute rest in bed and isolation with good nursing care are necessary

2 Diet is very important The diet should contain at least 2500 calories a day with a minimal amount of residue Carbohydrates should form the major portion since they are easily digested However at least 1 Gm of protein per kilogram of body weight is given with some fats Only fluids semisolids and soft foods should be included Milk cream butter eggs well cooked cereals sugar or glucose fruit juices chicken broth, and mashed potato may make up the major portion of the diet Anything that might cause perforation should be prohibited Stools should be inspected and if undigested curd is found it is a sign that too much milk is being given or that the function of the gastrointestinal tract is impaired At least 3000 cc of fluids must be taken daily If necessary they may be given parenterally

The diet should be supplemented by vitamins It is now believed that many of the complications and sequelae of typhoid fever formerly thought due to toxemia are in reality due to vitamin deficiencies

Vitamins A and D may be supplied in halibut liver oil and should be taken daily

Vitamin B complex may be administered in the form of brewer s yeast 30 Gm (1 ounce) daily If this cannot be taken the individual factors of the complex may be given separately Thiamin hydrochloride is given in doses of 2 to 10 mg daily by mouth or may be administered in solution 20 to 50 mg intravenously or intramuscularly daily The dose of riboflavin is 1 8 mg for a caloric intake of 3000 Calories Nicotinic acid is not advised as it increases peristaltic activity Liver extract 1 to 2 cc intramuscularly daily may be given and it supplies the B factors other than thiamin

The daily requirement of cevitamic acid in typhoid is 120 mg and it may be more This may be taken orally in amounts of 200 to 500 mg in 24 hours Citrus fruit juices also supply this vitamin If it is found by laboratory test that the blood level is below 0 5 mg per cent or a 24 hour urinary excretion level is below 30 mg then this vitamin should be given parenterally in daily doses of 500 mg

3 A high temperature may be relieved by sponge baths If the temperature is 39 5° C (103° F) or more these baths should be given every four hours Ice bags may be applied to the head and abdomen Alcohol rubs three or four times daily are of great benefit and keep the skin in good condition

4 A new horse serum is claimed to produce good results

5 Blood serum from typhoid carriers or transfusion of whole blood in amounts of 50 to 100 cc daily or every other day may be of value

6 Sulfanamides have not been of any proved value in treatment

7 If intestinal hemorrhages occur stop all food and fluid by *mouth withhold for a period of 24 hours or until evidence that* bleeding has ceased appears Ice chips may be given and the lips moistened frequently with a mixture of lemon juice glycerin and water Ice bags may be applied to the abdomen the foot of the bed should be elevated and morphine sulfate 0 011 to 0 016 Gm (⅙ to ¼ grain) hypodermically should be given A hypodermic injection of 100 units of parathyroid extract is of value in helping to increase the coagulability of the blood Calcium gluconate 10 cc of a ten per cent solution intravenously at four or five hour intervals is thought *to be of value If possible 500 cc of citrated blood should* be given Five hundred cubic centimeters of plasma may be given in lieu of this and hydration should be kept up by intravenous fluids 2000 to 3000 cc of five per cent glucose in normal saline solution

8 If constipation or flatulence is troublesome a low enema may be given

9 If perforation occurs immediate surgery is necessary Cases operated on within 24 hours recover much more frequently than those operated on later

10 Prophylaxis depends on

a Early recognition of the disease

b Isolation technic

c Disinfection of stools and urine

d Careful observation of food and water supplies

e Vaccination

f A patient who has recovered from the clinical phase of typhoid fever must have three negative cultures of the stool taken at three-day intervals before being released from isolation

g Carriers Recently iodophthalein has been reported by Saphir and Howell as effective in the treatment of typhoid paratyphoid carriers Four doses of 4 Gm (60 grains) each of iodophthalein were administered orally at weekly intervals and during a seven months period of observation the stools remained free from paratyphoid A organisms

Vaccine therapy may be tried in an attempt to cure the typhoid carrier and at times surgery may be advised

MENINGITIS

Meningitis is an inflammation of the membranes of the brain or spinal cord occurring most often in children Inflammatory lesions involving the meninges of the brain and spinal cord whether purulent tuberculous or serous present characteristic clinical signs and symptoms There is a group of meningitides caused by pus producing organisms of which the meningococcus is outstanding others as the staphylococcus streptococcus pneumococcus and gonococcus may cause the same kind of purulent infection Rather than take up the individual forms produced by various pyogenic organisms the meningococcic type of meningitis will be considered While other forms of purulent meningitis may not follow exactly the bacteriological pathological and clinical patterns of the meningococcic type they are quite similar from the diagnostic and therapeutic aspects Naturally from the prognostic angle they may be different Tuberculous syphilitic serous traumatic and other less common forms of meningitis will not be considered in detail here What is said in this chapter regarding the diagnosis and treatment of meningococcic meningitis may be applied to all of the purulent forms

Etiology Acute meningococcic meningitis is the commonest and most important form caused by the *Meningococcus intracellularis* While this organism may be found in the secretions of the nasopharynx of normal individuals it is not until the disease sets in that it is present in any great number This diplococcus is a gram negative type found intracellularly Why certain individuals are more apt to develop the disease than others is a question that remains unan

swered The disease may occur sporadically and attack persons in vigorous health In institutions the germ may be carried from one individual to another and an epidemic may break out

Pathology The disease is usually characterized by a systemic involvement with a positive blood stream culture before evidence of meningeal irritation appears The pia arachnoid over the base of the brain and spinal cord becomes involved, with the production of a thick purulent exudate This consists of fibrin and polymorphonuclear leukocytes which have the meningococci within them Sometimes the inflammatory process is widespread over the entire surface of the brain and spinal cord again it is more circumscribed

Signs and Symptoms The disease sets in abruptly and therefore must be differentiated from other infectious diseases that begin suddenly as pneumonia tetanus and streptococcal septicemia For a day or two before the appearance of the characteristic rigidity of the neck the patient usually feels irritable Headache and fever are present Sometimes the onset is so sudden that the first evidence noted is stupor delirium or even coma A brief inspection of the patient reveals stupor or semistupor which is not commonly seen in other acute infectious diseases The contrast between this clinical picture and that of the patient with pneumonia is sharp The latter is apt to be alert stimulated bright and usually has the typical anxious expression so characteristically lacking in acute meningitis Most patients with other infectious diseases are practically never so stuporous in the first few days of the disease Fever of 39° to 39 5° C (102 to 103° F) is a common finding and the blood leukocyte count usually ranges above 15 000 per cmm The patient may have scattered petechial hemorrhages especially over the ventral surface of the body These purpuric spots have been responsible for the name spotted fever applied at times to this disease The so called tache cerebrale may be seen on stroking the abdomen

Diagnosis The importance of a prompt and accurate diagnosis cannot be overemphasized especially at this time when specific chemotherapy is so effective The chief point in recognition consists in thinking of the possibility of acute meningitis When called to see a patient with an acute infection it is always a good habit to test the neck for rigidity and the legs for Kernig s sign The diagnosis is proved by examination of the spinal fluid which should be done

immediately The pressure is usually above 200 mm of water The fluid is turbid or even frankly purulent in advanced stages of the disease There is a great increase in the number of polymorphonuclear leukocytes 2000 or more cells per cmm may be present The sugar content of the spinal fluid is commonly reduced to less than 20 mg per cent The type of organism causing the meningitis can usually be readily determined though the etiological diagnosis is no longer so important since the treatment of all forms of pyogenic meningitis is much the same

TREATMENT

1 While the mortality rate in untreated meningococcal meningitis is about 85 per cent there has been a gradual decline since 1908 when Flexner reported his first series treated with specific antiserum While early administration of serum has met with some success this method of management of meningitis has not been highly satisfactory

2 Since the introduction of the sulfonamide group of drugs the mortality rate of meningitis has been greatly reduced The effect of these chemotherapeutic agents has often been dramatic Subsidence of symptoms with sterilization of the blood and spinal fluid has frequently been noted within 24 to 36 hours While relapses have occurred after the use of antimeningococcus serum practically none occurs after treatment with the sulfonamide drugs

Sulfanilamide sulfapyridine and sulfathiazole have all been used with fair success in the treatment of meningitis but sulfadiazine seems to be the drug of choice This drug is given in the following way 4 Gm (60 grains) orally as soon as the diagnosis is made followed by 1 Gm (15 grains) every four hours until the fever signs and symptoms have been controlled for 36 hours Sodium sulfadiazine in physiologic saline solution may be given intravenously to patients who cannot take the drug by mouth Three to 6 Gm (45 to 90 grains) of the drug may be given daily in this way Reports in the literature reveal that meningococcic meningitis responds satisfactorily to sulfadiazine in over 90 per cent of cases

The same precautions that have been sounded in the use of the other sulfonamide drugs must be recognized in the treatment with sulfadiazine The drug may cause vomiting and its sodium salt may have to be given intravenously in some cases The blood count

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⅓ grain) are necessary for the relief of pain and restlessness These depressants should be used with caution however as pneumonia may ensue

9 In pulseless fulminating cases epinephrine 0 6 to 1 22 cc (10 to 18 minims) intramuscularly or intravenously every four hours according to the pulse may be tried as an emergency measure.

ACUTE EPIDEMIC ENCEPHALITIS

This is an acute infectious disease the cause of which is unknown characterized clinically by nervous system disturbances

Pathological Anatomy The brain is usually hyperemic and tiny hemorrhages occur in the meninges and in the brain particularly in the area of the basal ganglia Vascular congestion with perivascular lymphatic infiltration with edema are characteristic Sometimes small necrotic patches are found Hydrocephalus generalized edema of the brain petechial hemorrhages tiny areas of necrosis congestion and lymphocytic infiltration are the main features found at autopsy

Signs and Symptoms Generalized involvement of peripheral nerves lethargy meningeal symptoms stupor and coma are the main features All cases do not run true to this pattern Sometimes in place of lethargy there is violence and in place of stupor and coma there are irrationality and jactitation

Encephalitis may appear sporadically or there may be epidemics of it The disease is rare in children and in older people it occurs most commonly in young adults under the age of 40 The onset as a rule is acute and there is fever headache general malaise vomiting and other variable features that characterize the early period of any acute infectious disease During the first day or two the condition may be confused with influenza or ordinary upper respiratory infections After the first few days the fever rises higher the patient becomes irrational lethargic or noisy and finally certain characteristic evidences of brain involvement make their appearance There may be twitchings or choreiform movements of the arms and legs double vision and paralysis of certain muscles of the eyeball may appear Sometimes there are mild clonic movements particularly involving the abdominal muscles The persistence of these unusual manifestations quickly indicate that the patient has something more than the flu

must be watched for the development of agranulocytosis The urine must be studied for evidence of renal insufficiency These unfavor able reactions however are less likely to occur with sulfadiazine than with sulfanilamide sulfapyridine or sulfathiazole As sulfadiazine is more readily absorbed than some of the other drugs of this group it is possible to obtain a satisfactory blood level of from 10 to 15 mg per cent within eight hours If the blood level fails to rise above 3 mg per cent within this time one should not hesitate to give 3 to 5 Gm (45 to 75 grains) of sodium sulfadiazine intravenously at once and to continue giving it every day until the disease is controlled

3 Penicillin is used in the following manner 10 000 to 20 000 units in 10 cc of sterile isotonic saline solution is injected intra spinally after 10 cc or more of spinal fluid is withdrawn The dose is repeated at ten hour intervals for from three to five doses and then one dose in 24 hours is given until recovery is assured The number of intraspinal injections needed depends upon the condi tion of the patient Usually about 100 000 units are required to control the disease Simultaneously intramuscular injections of 10 000 units of penicillin is given every three hours and continued until there is definite improvement The usual period of intra muscular therapy is from three to seven days and the total amount given varies from 180 000 to 500 000 units Even more successful results follow combined sulfonamide and penicillin therapy than follow therapy with either drug alone

4 It is preferable that the patient be hospitalized

5 Fluids should be pushed A liberal diet high in calories and vitamins should be given as soon as the vomiting has subsided Forced feeding may be necessary when a tendency to chronicity develops

6 In some instances catheterization may be necessary for a short period The urinary output should be watched closely and means other than catheterization used to secure relaxation of the bladder sphincter

7 A cleansing enema should be given daily

8 For the relief of the severe headache sodium bromide 0 66 to 1 Gm (10 to 15 grains) three times a day may be given but in the early stage of the disease the narcotics morphine sulfate 0 011 to to 0 016 Gm (1/6 to 1/4 grain) or pantopon 0 011 to 0 022 Gm (1/6 to

bromide is given by mouth beginning with a dose of 0 0003 Gm (1/00 grain) three times a day This dose must be increased as the patient develops a tolerance for it Many patients require 0 0013 Gm (1/0 grain) three or four times a day Tincture of stramonium may be given in a dose of 0 66 cc (10 minims) three times daily and increased either by 0 066 cc (1 minim) a day or by 0 33 cc (5 minims) per dose per week until a maximum dose of 8 cc (120 minims) three times a day is reached The unpleasant symptoms which develop such as drying of the throat blurring of vision and mental confusion may make the treatment of questionable value When discontinuing the drug it should be done gradually

POLIOMYELITIS

Acute poliomyelitis (Heine Medin disease) is an acute infectious contagious disease characterized typically by symptoms referable to changes in the anterior horn cells of the central nervous system

Etiology The specific etiology of poliomyelitis is a filterable virus Its portal of entry is still debated The larger school believes that the virus enters the central nervous system directly from the nasopharynx particularly by the olfactory nerve The disease has been recently classified simply into (1) The abortive type which is not diagnosed except by elaborate experimental study (2) the non paralytic type (3) the lower motor neurone type both spinal and bulbar (4) the encephalitic type—rare and (5) the ataxic type—very rare Mixed types may occur The disease has been considered one of childhood but recently greater incidence has been reported in the older age groups The ratio of males to females is 3 to 2 Negroes appear to be less susceptible than white people Recognizable cases occur largely in the temperate zone The disease is most prevalent during spells of hot dry weather but may appear at any time of the year One attack of the disease appears to confer lasting immunity

Pathology Congestion and edema are present in the entire nervous system more marked in the cord and brain stem than in the brain proper Most of the pathological changes are found in man in the lumbar segments of the spinal cord the cervical region is affected next in order of frequency The first notable changes are in the vessels of the anterior horn which become congested distended and sur

The examination of the patient may reveal rigidity of the neck paralysis of some of the cranial nerves periodic attacks of dyspnea or apnea and a generalized rigor of the muscles of the legs and arms

Poliomyelitis meningitis cerebral thrombosis or hemorrhage, uremia and rupture of a mycotic aneurysm of vessels of the brain must all be considered A spinal puncture may show practically no evidence of disease An increase of the glucose content above 90 mg per cent is suggestive of encephalitis while in pyogenic forms of meningitis the glucose content is well under 50 mg per cent Sometimes there is an increase of the cell count but not always

Prognosis The outlook for a patient with the various kinds of acute encephalitis is not good There is a mortality rate of about 20 to 30 per cent Sudden bradycardia or an acute respiratory paralysis may quickly terminate the patient s life When these patients recover the recovery is apt to be more apparent than real in some cases for a number of years later the individual may develop a post encephalitic Parkinson s syndrome

TREATMENT

The treatment may be classed into general and special measures The general measures consist in protecting the patient from intercurrent infection and injury keeping up nutrition watching for distention of the bowels from obstipation and carefully preventing overdistention of the urinary bladder and urinary tract infections

Special Measures Repeated lumbar punctures and intravenous administration of hypertonic glucose 50 cc of a 20 per cent solution daily or twice daily are used to control high spinal fluid pressure if it exists The sulfonamides appear to be of no value in encephalitis The specific antiserums seem to have little effect The reported results of the therapeutic antiserums are conflicting so one may assume that their value is strictly limited Finally in the management of a patient suspected of encephalitis of the acute epidemic type isolation measures for the protection of those around the patient must be carried out

In the chronic stage attention should be given to the eradication of any foci of infection paying particular attention to the sinuses Massage and hydrotherapy are useful Drugs may relieve the symptoms but do not arrest the progress of the disease Hyoscine hydro

If paralysis occurs it is practically always flaccid and most often develops on the second or third day The paralysis usually reaches its maximum almost immediately but additional paralysis may develop over a period of several hours to as many days Any group or any combination of groups of muscles may be affected The degree of involvement varies from weakness to complete loss of power Death is practically always due to respiratory failure associated with increasing paralysis of muscles of respiration

Diagnosis In the majority of cases the spinal fluid is increased in amount and shows an increased cell count to as high as several hundred Mononuclear cells predominate as a rule although at times predominance of the polymorphonuclear cells is seen The protein is usually slightly increased The sugar is normal or high The blood count is not characteristic

Prognosis The seriousness of the disease can be overrated There are many abortive cases A large percentage of cases are diagnosed that develop no paralysis at all Many of those patients who develop paralysis recover with little or no disability if adequate care is given There is little danger of behavior disturbances and of mental deterioration

TREATMENT

1 Poliomyelitis is a quarantinable disease the minimum period of quarantine being three weeks During the course of an epidemic it is advisable that all cases of indefinite illness in children under five years of age especially if fever diarrhea cough and vomiting are present should be treated as positive cases of infantile paralysis

2 Bed rest and all the fine points of nursing technic are essential in the acute stage

3 The infection should be controlled at the point of entry by means of argyrol 25 per cent or hydrogen peroxide applied with a postnasal spray

4 Convalescent serum has been used but the results have not been convincing

5 During the acute phase the bowels should move at least twice a day Enemas may be necessary a very satisfactory one consists of giving 120 cc (4 ounces) of warm olive oil to be retained one hour or more then followed by 1000 cc (one quart) of soapy water If this method fails follow by an enema of magnesium sulfate 60 cc

rounded by small cell infiltrations The gray matter is particularly affected but the meninges and white matter are also involved The nerve cells may die quickly with little alteration of cell outline but with swelling of the nucleus coagulation of Nissl bodies and gradual disintegration of the cytoplasm of the cells or there may be necrosis of the nucleus disappearance of the Nissl body and evidence of active phagocytosis of nerve cells Degenerative changes can be traced into the anterior roots Later the motor nerve trunks show decrease in size and number of their fibers The anterior horn as a whole becomes sclerosed and shrunken Muscles become pale and flabby atrophy is early and marked Extensive hyperplasia of lymphoid tissues is described

Signs and Symptoms The incubation period varies from 6 to 18 days The initial symptoms are quite the same in all types of the disease except the abortive and they may be quite as severe in the nonparalytic as in the paralytic form The onset is usually abrupt Early symptoms are headache fever vomiting constipation or diarrhea and frequently congestion of the throat The temperature usually is from 37 8° to 39 5 C (100° to 103° F) without characteristic curve Usually the fever lasts not more than ten days and generally falls by lysis The pulse is rapid in proportion to the fever A more rapid pulse suggests early bulbar involvement Hyperesthesia is often seen early It is usually more marked along the spine and over the large nerve trunks and is demonstrated by somewhat deep pressure Diminution of sensation almost never occurs There is often pain in the neck back extremities or abdomen The abdominal pain may resemble that of the surgical belly The duration of pain is usually short but occasionally the necrotic pains may be long standing Drowsiness alternating with irritability when disturbed is common Delirium is rare Twitchings of groups of muscles are occasionally seen early Ataxia is rare convulsions are infrequent Evidence of meningeal irritation occurring early is stiffness of neck and back and often a positive Kernig and Babinski sign Reflex changes are important Early the deep reflexes are exaggerated and equal A positive Babinski or ankle clonus may be present temporarily The deep reflexes may become unequal diminished or lost Superficial reflexes are present unless the underlying muscles are paralyzed The pupils are not affected There may be difficulty in voiding urine

commoner in tropical countries it occurs in the United States especially along the Eastern seaboard during the summer months

Etiology Tetanus usually follows an injury Lacerated wounds of the hands or feet caused by contaminated nails or splinters and gunshot or shrapnel penetrations are the most frequent causes of the disease A high incidence is due to burns incurred in 4th of July accidents Occasionally the B tetani enters the body during operation on the rectum or perineum Any laceration of the skin or tissues may be the source of infection and consequently careful first aid treatment should be given any punctured wound Probably the most dangerous wounds are those received in cultivated fields street and road accidents about animal barns and those in which foreign bodies or sequestra are left

The B tetani is a drumstick shaped organism with a terminal spore It is slender slightly motile in the vegetative form and usually grows singly It is most often described as an obligatory anaerobe which is gram positive in its staining properties and grows at but 37 5 C in a slightly alkaline medium devoid of oxygen It produces an exotoxin which is especially harmful because of its affinity for the central nervous system

Signs and Symptoms The incubation period varies from one day to three or four weeks depending on the length of time required for the toxins to travel along the nerves to the centers It may be prolonged if antitoxin is given to prevent tetanus Symptoms are absent during this period and the wound in which inoculation has occurred may be forgotten

The first indications of infection usually consist of headache and general depression Active symptoms may begin with stiffness in the mandibular joint on opening or closing the mouth difficulty in swallowing or chewing restlessness irritability and frequent yawning Sometimes chills or rigors occur and the muscles nearest the wound may show spasticity Stiffness of the neck arms or legs headache fever and chills may be observed These signs appear a few days after the injury and if they are recognized as the premonitory signs of tetanus therapy may be instituted immediately and the patient will have a better chance for recovery

Later the neck becomes rigid Tonic spasm of the masseter muscles causes trismus or lockjaw and the mouth becomes distorted in a

(2 ounces) glycerin 10 cc (2 ounces) and warm water enough to make 500 cc (one pint)

6 The diet should consist of milk plain diluted or modified broths modified cereals if much gas is present and fruit juices The patient should drink plenty of water and if refused warm saline solution should be given rectally Vitamin C 25 to 50 mg twice a day and B_1 10 000 units daily are recommended Their efficiency is problematical but they can do no harm If there is difficulty in swallowing feeding must be forced by stomach tube

7 When fever is high sponge baths or cool enemas should be given Ice cap may be applied to the head Lumbar puncture is frequently of value when there are signs of meningeal irritation and may be done repeatedly Increased intraspinal pressure may also be relieved by hypertonic glucose solution 50 cc of a 50 per cent solution intravenously once or twice daily

8 In the polyneuritic type a suppository of opium 0 033 Gm (½ grain) extract of belladonna 0 008 Gm (⅛ grain) and sodium salicylate 0 33 Gm (5 grains) should be administered every three hours until pain is relieved

9 If stupor is present a hot mustard pack should be applied The patient should drink water or grape juice while in the pack and should be rubbed dry after the pack

10 Perivascular drainage continues to be advocated occasionally but apparently the virus cannot be washed out

11 A respirator should be on hand at all times to be used in the event of respiratory paralysis

12 Orthopedic care as pads splints or casts is given as support to weakened or paralyzed groups of muscles

13 To date it has been emphasized that weakened muscles be protected from attempts at motion However the Kenny treatment of a firm mattress supported by bedboards hot foments to the affected muscles passive movements through the range of motion possible without pain and muscle training is receiving wide publicity its value may be proved

TETANUS

Tetanus (lockjaw) is a specific infectious disease caused by the *Bacillus tetani* which produces a powerful toxin It is characterized by intermittent painful tonic spasms of the muscles Although it is

Prognosis Recovery occurs in about 45 per cent of cases Age site of wound length of the incubation period and the abruptness of the period of onset all play a part in prognosis Tetanus in the very young and in older patients is usually fatal If the infected wound is on the face or neck or if the symptoms are severe the disease is likely to be fatal If the period between inoculation and the first symptom is more than ten days prognosis is good but if it is less than a week prognosis is bad However the nature of onset is important too If onset is insidious or more than four days chances for recovery are very good while if it is abrupt or less than two days the disease will undoubtedly be fatal no matter what treatment is used

TREATMENT

1 **Prophylactic**

a Thorough cleansing of the wound is necessary
b If infection is suspected 5000 to 10 000 units of antitoxin should be given intramuscularly or subcutaneously
c One cc of tetanus toxoid may be given deeply subcutaneously and followed in six weeks by another injection of the same amount This treatment is preferable to the antitoxin because it actively immunizes the patient against tetanus and causes little discomfort

2 **Curative** There have been many programs advocated in treating tetanus The following regime appears to be the best one for most cases To a large extent it is the method reported by Vener and Bower

a A serum test for sensitivity is done
b The patient should be kept in a quiet darkened room to soothe the irritated nervous system
c Chloral hydrate is given orally or if the patient is unable to swallow a retention enema of this drug with the same amount of calcium bromide is given The dose varies from 0 33 to 2 Gm (10 to 30 grains) dependent on the size and age of the patient This dose may be repeated if necessary
d An hour later administration of antitoxin should begin Twenty thousand units are injected completely around the wound If possible this area should be anesthetized previously
e One hour later 60 000 units of antitoxin should be injected intramuscularly at the proximal extremity of the part involved so as to control the progress of the toxin Then the focus should be incised widely or excised thoroughly care being taken to keep within the circle formed by the antitoxin injections All foreign material should

sardonic grin As a result of involvement of the facial muscles the mouth cannot be opened and efforts to do so cause great pain Gradually the process involves all the muscles in the body The abdominal and lumbar muscles reveal boardlike rigidity The back may be so stiff that the patient rests on his head and heels during a spasm The entire trunk and limbs may be rigid

The most characteristic features of general tetanus are rigid locking of the jaws and painful convulsions which may be precipitated by jarring or handling of the patient or any irritation These spasms occur with increasing frequency and can be precipitated by the slightest stimulus They may be local or general in character and may be momentary or last for a few minutes but relaxation is not complete between attacks During these spasms the patient usually perspires profusely When death occurs during a paroxysm it is due to exhaustion suffocation or heart failure

The terminal stage of the disease develops during the second week Unfortunately the patient remains mentally alert until death *The pain grows more intense and convulsions are more frequent* urinary retention high fever sweating and exhaustion usually precede death

Diagnosis Careful history and examinations will usually differentiate tetanus from diseases with which it might be confused A history of injury plus a B tetani culture from pus or tissue of the wound are very important in diagnosis Rabies strychnine poisoning tetany hysteria and meningitis may make the diagnosis questionable Rabies follows a dog bite A history of having taken the drug or its recovery from the intestinal contents are necessary for the diagnosis of strychnine poisoning The muscles of the jaw are seldom involved in this *poisoning* and there is complete relaxation between spasms In tetany the involvement of the hands with fingers outstretched and the thumb turned under the palm the absence of rigidity of the jaws *and lumbar muscles* and the peculiarity of the position of the patient distinguishes it from tetanus A lumbar puncture is valuable if meningitis is suspected At all times a culture of B tetani found in the tissues at the portal of entry proves *the diagnosis of tetanus* Impaction of an infected third molar tooth may present symptoms suggestive of tetanus but swelling of the face and pain on pressure over this tooth and the second molar make the diagnosis *comparatively easy*

CHAPTER XX

Acute Infections

(Continued)

PSITTACOSIS

Psittacosis is an acute infectious disease of man resulting from contact with parrots or laboratory animals infected with the virus of psittacosis The disease is characterized by severe toxemia with a peculiar bronchopneumonia and symptoms suggestive of typhoid fever

Etiology Many organisms have been reported as causes of psitta cosis However the disease has been proven to be due to a filtrable virus since the etiologic agent may be passed through Chamberland and Seitz filters

Pathology The changes found at autopsy are those of a general septicemia with a peculiar inflammatory picture in the lungs The lungs are usually uniformly congested and swollen and are red to dark purple and boggy Purulent material may be exuded from the bronchi There may be lobular or lobar consolidation Microscopi cally various stages are described (1) A hemorrhagic vesicular pneu monia with proliferation and desquamation of the alveolar walls (2) an increase in engorgement with much serous exudate containing few leukocytes (3) development of a fibrinous exudate containing many small round cells as well as large multinucleated cells There is a variable degree of bronchitis Perivascular infiltration in the brain as well as serous meningitis have been described The organs of the body show cloudy swelling as a result of severe toxemia

Signs and Symptoms The disease may occur at any age or in either sex The incubation period varies from 5 to 21 days The ill ness usually begins with fever chilly sensations and general malaise There may be a photophobia and frequently a splitting headache In spite of the fact that the patient has a temperature of 39 5 to 40 C (103 to 104 F) for the first few days he may feel quite well and the pulse is usually relatively slow During the early stages of the disease there are usually morning remissions of the fever Ano-

be removed from the wound and hot compresses of potassium permanganate should be applied.

f Two or three hours later cisternal puncture should be done removing about 10 cc. of fluid and injecting slowly by gravity 20 000 units of antitoxin heated to body temperature This procedure causes the temperature to rise but in six or eight hours it recedes without undue effects

g When the temperature has receded to 39 C (102 F) 0 33 cc. (5 minims) of epinephrine should be given hypodermically followed in five minutes by the slow intravenous injection of 40 000 units of antitoxin diluted in 300 to 500 cc. of physiologic solution of sodium chloride Epinephrine hypodermically should be repeated in the middle period of the antitoxin injection and following it If the antitoxin is kept at room temperature for 24 hours before using and heated in a lukewarm water bath just before injection serum reactions are less likely to occur

h Two hours after completion of the above injection 1 Gm (15 grains) *of methenamine should be given intravenously*

i About an hour later another 20 000 units of antitoxin should be given intravenously in 300 to 500 cc. of physiologic solution of sodium chloride Precautions against serum sensitivity and anaphylactic shock *must be taken If the patient has had any untoward reactions* from the first injection the second is withheld About 12 hours later the final 40 000 units of antitoxin is given deeply intramuscularly and proximal to the site of the previous injection This dose is increased *to 60 000 units if the intravenous injection has been omitted* About ten hours after this injection methenamine is given as before

j The total dose of 200 000 units of antitoxin has now been given The ordinary prophylactic dose of 1500 cc should be given every four or *five days for four doses to maintain the serum desensitization* of the patient

k Sodium amytal 0 4 to 0 6 Gm (6 to 9 grains) by mouth or rectum should be given to control spasms

l *In severe cases or those in which the prognosis is bad 0 1 Gm (1 5 grain)* of avertin per kilogram of body weight should be injected rectally and repeated every four to six hours if spasms recur

m If the patient perspires profusely and dehydration occurs sodium *chloride should be replaced Since the muscular exertion* of the patient is great he must be well fed If he is unable to take anything by mouth it is wise under anesthesia to pass a fine stomach tube through the nose so food may be given The very act of swallowing may be dangerous because *it may initiate a spasm*

n Oxygen should be administered if cyanosis is present

o Pneumonia should be guarded against

serum for more than a year in some of the convalescent cases A positive Wassermann may give positive complement fixation reaction for psittacosis Nonspecific fevers never caused elevating titers nor titers above 1 to 8 in my experience

Prognosis Psittacosis is a serious infection Various observers have reported mortality rates from 8 to 45 per cent The most important factor in prognosis is age The disease is a very serious threat to life in older individuals The disease lasts from two to three weeks If patients are going to die they usually do so during the second week they become extremely toxic with extensive pulmonary involvement and expire

TREATMENT

The treatment of psittacosis is mainly symptomatic and palliative Meyers differentiates between two antibodies produced by the virus of psittacosis (1) The complement fixing antibody which is utilized in the diagnostic test and appears early in the disease and (2) a virus neutralizing antibody appearing later in the disease Serums high in this virus neutralizing antibody may be effective in the treatment of psittacosis One case is cited in which a crisis is produced by immune serum with a high titer of virus neutralizing antibodies Meyers has also prepared hyperimmune goat serum Hinshaw of the Mayo Clinic reports two cases treated with sulfapyridine both of which recovered The general treatment of psittacosis may be outlined as follows

1 The patient should be isolated and in surroundings as quiet as possible as excitement tends to make the headache and delirium worse

2 A full diet can and should be given with the exception of stimulating and irritating foods Large amounts of fluids may be given

3 Acetylsalicylic acid 0 66 Gm (10 grains) four times a day or phenacetin 0 33 Gm (5 grains) three times a day should be given in an attempt to relieve the headache which is usually the chief concern of the patient Narcotics as morphine sulfate 0 008 to 0 016 Gm (⅛ to ¼ grain) hypodermically may have to be resorted to but should be given only in exceptional cases

4 Tepid baths or alcohol sponge baths may be necessary to reduce the fever

fever vomiting sore throat and herpes may appear quite early In from three to seven days findings of pulmonary involvement are usually present

As a rule, the physical findings manifest themselves in the bases of the lungs first Only a few rales may be heard at first but later signs of consolidation patchy in character may appear The patients rarely show *the marked increase in respirations or the cyanosis* so often associated with other types of pneumonia There may be a persistent cough but the production of sputum is usually minimal In many cases the patient appears quite well about the eighth day only to have a continuation of the pneumonic process with resultant toxicity and fever for several more days During this period small pink oval papular skin lesions may appear on the trunk These lesions fade on pressure and develop a white halo on rubbing Typically the disease lasts from 10 to 14 days with the fever ending by lysis Fulminating cases may occur with the development of a typhoid state delirium diplopia hallucinations and stupor The urine often *shows albumin with no other findings* Relative leukopenia with a shift to the left is common There is usually no marked leukocytosis or lymphocytosis Recovery from the disease is slow the cough and lung findings disappearing gradually The patient may *remain in a* weakened condition for weeks The commonest complication is phlebitis of the femoral vein Parotitis and ulcerative stomatitis occur rarely

Diagnosis The diagnosis is suggested by a history of contact with parrots or parakeets Clinically the disease simulates influenza or typhoid more closely than any other infectious disease The acute onset with severe headache and malaise may cause one to entertain a diagnosis of influenza Hacking cough associated with a relative bradycardia frequently brings typhoid to the clinician s mind The diagnosis may be clinched by injecting mice with sputum from the patient and demonstrating the intracellular coccobacillary bodies in the spleen or liver after the mouse dies Blood serum may be sent to the Williams Hooper Foundation in San Francisco where the specific complement *fixation test is done This test becomes* positive as early as the sixth day of the disease It should be repeated during the course of the disease and if the antibody titer rises this is almost pathognomonic for psittacosis The antibodies *are present* in the

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4 Tepid baths or alcohol sponge baths may be necessary to reduce the fever

5 The distressing cough is ordinarily not relieved by the usual mixtures and codeine sulfate 0 016 to 0 033 Gm (¼ to ½ grain) may be administered With laryngitis as a complication warm steam *inhalations with compound tincture of benzoin added to the* water are of benefit

6 The perichondritis in the nose may be relieved by application of zinc oxide ointment or yellow petrolatum

7 Luckie feels that massive doses of leukocytic extract, 5 cc *given hypodermically* or intramuscularly every four hours day and night are indicated and influence the disease remarkably

Convalescence requires careful consideration as relapses are common and phlebitis may and is likely to develop If the case has been severe, the patient should live quietly for 30 days after the temperature drops and resume exercise and labor very slowly

TULAREMIA

Tularemia is an acute specific infectious disease caused by the Bacterium tularense It occurs in animals especially the rabbit and rodents and in human beings

Etiology The Bacterium tularense is a short rod shaped non motile, gram negative bacillus Man acquires tularemia by direct contact with animals particularly rabbits or squirrels or through blood sucking insects infected through these animals Wild rabbits are chiefly responsible for the disease in human beings Infection is most often acquired through handling skinning or preparing the *animals for cooking*

There are four main types of the disease which are usually dependent on the manner in which the disease is contracted (1) The ulceroglandular which is the commonest (2) glandular (3) oculo glandular and (4) typhoid or intestinal forms The typhoid type, *which is the rarest* is difficult to diagnose because there is no primary lesion or glandular involvement to be seen and because it resembles gastrointestinal disease

Signs and Symptoms The period of incubation is usually one to five days Onset is sudden with headache fever chills and general aching This is followed by loss of weight prostration glandular symptoms vomiting sweating and weakness The lesion of ulceroglandular tularemia is quite characteristic there is a painful papule

at the site of the infection which usually breaks in a day or two releasing a necrotic sore The lesion is a small ulcer with a raised edge The regional lymph nodes are painful and usually enlarged Hyperglycemia is usually present but there is an absence of leukocytosis The primary ulcers may so closely simulate an ordinary abscess that they may be cut open and drained in error This makes a bad matter worse and often spells disaster for the patient

The glandular type is like that described above except there is no primary lesion In the oculoglandular form the lesion is on the lower eyelid with involvement of the lymph nodes pain and swelling The typhoid type results from eating rabbit meat that has not been cooked properly There is an absence of the primary lesion and regional lymph node involvement but there is severe epigastric pain vomiting diarrhea and enlargement of the anterior cervical lymph nodes Typhoid tularemia is sometimes mistaken for undulant fever

Diagnosis Diagnosis may be clinched by a history of dressing or eating wild rabbits isolation and identification of the bacillus localized lesion glandular swelling and agglutination of the patient s serum with *Pasteurella tularensis* Diagnosis should be made clinically first as the agglutination is not usually positive for two or three weeks and often longer It may be confirmed by culture from inoculated guinea pigs or by an intradermal test with a specific antiserum

Prognosis Most uncomplicated cases of tularemia recover though convalescence is a prolonged process often a year elapses before the patient feels like himself Cases of death from tularemia have been reported as due to glandular enlargements rapidly developing septicemia and focal necroses in the liver spleen lymph nodes bone marrow and lungs Meningitis and pulmonary complications usually end fatally

TREATMENT

1 The patient should be put to bed and suppurating lymph nodes drained

2 Ice bags or hot water bottles applied to the painful lymph nodes usually relieve the pain

3 Treatment is usually symptomatic though there is a specific treatment for the disease Foshay s serum 15 cc twice daily on alternating days has proved to be quite successful in bringing about symptomatic relief and cutting the death rate

5 The distressing cough is ordinarily not relieved by the usual mixtures and codeine sulfate 0 016 to 0 033 Gm (¼ to ½ grain) may be administered With laryngitis as a complication, warm steam inhalations with compound tincture of benzoin added to the water are of benefit

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number of cases have been seen in Texas Iowa and other midwestern States

Signs and Symptoms Brucellosis is difficult to describe because it presents so many symptoms and signs common to other infectious diseases Typhoid fever tuberculosis acute rheumatic fever acute endocarditis tularemia and influenza are commonly confused with brucellosis

Just as the incubation period ranges from 2 to 10 or 12 weeks so too do the clinical signs vary in character and severity The onset may be sudden or insidious with acute upper respiratory symptoms and the disease usually continues for about three months Fever weakness and drenching sweats are the outstanding clinical features A multiplicity of other symptoms seen in any infection may develop

Spondylitis is probably the commonest complicating disorder of the bones and joints referable to undulant fever Most authors agree that spondylitis as a complication of undulant fever is most likely to occur several months after the onset of the febrile state but cases of brucellosis have been reported in which localization in the spinal column developed as early as three weeks and as late as one year after the original infection The patient may even appear to have recovered from the systemic disease only to become affected by the spinal complication at some later date

Diagnosis The examination of the patient as a rule fails to reveal any evidence of disease commensurate with the fever and other symptoms Frequently the patient feels unusually well notwithstanding the fact that the fever may be 39 5 C (103 F) The differential diagnosis is difficult because so many other conditions may produce a similarity of symptoms After tuberculosis syphilis endocarditis malaria and typhoid fever have been eliminated as causes of the fever special laboratory procedures must be used to make the diagnosis of brucellosis The diagnosis is clinched if one can grow the organism from the blood and identify it In acute brucellosis agglutination tests and skin tests are helpful but not so in the more chronic cases A positive agglutination test does not mean the patient is suffering from brucellosis at the time the test is positive These tests too may be negative in some persons who have an active disease

Leukopenia occurs in most patients and the lymphocytosis with a high ratio of immature lymphocytes is common Other laboratory

4 Sulfadiazine 1 Gm (15 grains) four times daily has been given with some success Powers and Powers achieved favorable results with the combined treatment of sulfanilamide and antiserum

5 Sodium salicylate 1 2 Gm (18 grains) dissolved in 30 cc of water given intravenously twice daily seems to be beneficial

6 Streptomycin has proved a successful method of therapy in the treatment of tularemia although to date the initial amount given may be considered inadequate in the light of current knowledge of organism sensitivity

7 Other remedies include

a Bismuth sodium tartrate 2 cc of a three per cent solution
b Quinine sulfate 0 33 Gm (5 grains) three times a day for two weeks
c Metaphen intravenously in dilution of 1 1000 in doses of 10 cc every other day for three injections or in severe cases 10 cc. daily for four days and repeated on alternate days for three more injections
d Frontylin in 10 cc. doses four times daily until cyanosis begins and then repeated a week later

8 Preventive measures are important and may be listed as follows

a Rabbit hunters and eaters should avoid rabbits that are easy to catch they are probably diseased
b When dressing wild game the hands should be protected especially if there are open lesions or cracks on the hands
c Wild game must be thoroughly cooked
d Ulcerative lesions developing on the hands or face after the person has handled wild game should suggest tularemia and treatment should be instituted immediately

BRUCELLOSIS

Brucellosis is a focal or systemic infection usually caused by the ingestion of raw milk containing Brucella though there are other avenues of infection as the skin mucous membranes or the gastro intestinal tract It is principally a disease of young adult males who work on farms in packing houses or butcher shops The most important factor in the control of the disease is the pasteurization of all dairy products especially milk Although man contracts the disease from animals so far as is known it is not transmitted from man to man Brucellosis is uncommon in the United States though quite a

number of cases have been seen in Texas Iowa and other mid western States

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aids, as the sedimentation rate and erythrocyte count, are of less importance Although some patients die of the disease fatalities are rare Sometimes intercurrent conditions as pneumonia tuberculosis and other infections are responsible for the death of the patient While fatalities are rare *morbidity is prolonged and constitutes one of the most unfavorable features of the disease the disease may last* from six weeks to several months

TREATMENT

The treatment may be classed into the symptomatic or general and the special therapeutic agents

1 Symptomatic treatment requires that the patient be kept in bed and that the caloric requirements of the body be furnished by an adequate diet The other simple methods used to relieve distressing symptoms and to make a patient comfortable are employed

2 The special agents are serum vaccines and brucellin

a Antibrucella serum has given very favorable results especially in the acute cases If the diagnosis is positively made about 20 cc of serum *is given intravenously each day on three successive days* and the clinical response is usually quite dramatic

In very severe cases 90 to 120 cc may be given in unit doses of 30 cc during 48 to 72 hours Daily doses of 10 cc each may be given intramuscularly or subcutaneously until 20 or 30 cc have been administered Serum therapy is *not* indicated in chronic cases of more than eight months duration unless sudden severe exacerbations occur

b Vaccine therapy has been followed by more indefinite results than serum therapy Within recent years better preparations have been used and some of the former difficulties have been overcome to some extent Fxperience and good judgment are the essential requisites in determining the proper dosage Usually a test is performed for hypersensitiveness to the vaccine—0 05 cc of a 1 10 dilution of the vaccine is injected into the deep subcutaneous tissues or the muscle If there are no reactions a second such dose may be given three days later The dosage is then increased by 0 25 cc at intervals of three days until a total of 1 cc is given *Five to eight injections of 1 cc* each may then be administered at three day intervals If a severe reaction occurs during the course of treatment the following dose should be reduced to one half that which caused the reaction and the succeeding doses may be gradually increased A series of four to six or more sharp systemic febrile reactions usually accompanied by a transient exacerbation of symptoms is the goal to strive for Only extreme local or general reactions should be avoided

c Brucellin is obtained from the brucella cells grown in liver broth The bacteria free active agent is obtained from the liver broth filtrate The patient is tested out for sensitivity by giving an intradermal injection of 0 1 cc of brucellin and if the patient is nonsensitive 1 cc is given hypodermically at three day intervals until the morning and evening temperatures between the intervals of injections tend to become sub normal Here too the object of therapy is to produce a series of four or more febrile systemic reactions

d Treatment of brucellosis could hardly be passed over without mention of the sulfonamides Experience has shown that no sulfonamide has given very satisfactory results Neoarsphenamine mercurochrome acriflavine metaphen gentian violet and other substances have been employed in the care of these patients but their value must be regarded as undetermined until more work is done Injections of foreign pro tein substances as typhoid vaccine and sterile skimmed milk have been used with some degree of success Artificial fever therapy in the man agement of these cases has been quite effective The usual course of therapy is six fever sessions each of three hours duration at a rectal temperature level of 40 5 C (105 F) given during a period of two weeks Especially good results have been obtained in patients who did not respond to vaccine therapy

e Aureomycin has been reported of distinct value in the few cases reported

f Within recent times colloidal manganese has been used successfully in some stubborn cases This preparation is given in 10 cc doses intravenously every two or three days for two weeks and then twice a week for about six weeks

g In patients in whom high blood levels may be maintained strepto mycin has proved highly responsive Therapy at high dosage how ever is not without risk of streptomycin intoxication

RABIES (HYDROPHOBIA)

Rabies is an acute infectious disease of warm blooded animals especially dogs It is characterized by terminal paralysis convulsive seizures and a fatal outcome which is often preceded by coma

Etiology Human beings acquire the disease when they are bit ten by a rabid animal or when a human abrasion is licked by the ani mal The etiologic agent of rabies is questionable it is most often referred to as a virus yet it may be a protozoan organism with cell inclusion bodies Negri found that certain rounded eosinophil bodies occupy the interior of the nerve cells in most cases but it is not known if these cause the disease or are merely the result of it The

virus of rabies is filtrable and is contained especially in the saliva it spreads up the peripheral nerves to the central nervous system

Signs and Symptoms The incubation period varies from two weeks to two months depending usually on the proximity of the site of infection to the central nervous system The average incubation time is about six weeks When the patient first shows signs of the disease there is irritation around the scar of the bite as well as severe pain The early symptoms are associated with the central nervous system and are those of severe encephalitis The patient complains of headache difficulty in swallowing and loss of appetite He is irritable sensitive and unable to sleep Usually a slight rise in pulse and temperature is noted Several days later the stage of excitement sets in and the patient becomes restless excitable and has maniacal tendencies He experiences reflex paroxysms of pain and when he attempts to swallow he is conscious of painful spasms of the muscles of deglutition and respiration There is frothing at the mouth and vomiting most often of a bloody saliva The fever rises to 38 3° to 39 5° C (101 to 103° F) the pulse increases in rate with each convulsion Shrieks of terror and wideopen mouth are characteristic of the pharyngeal spasm Patients are unable to swallow and efforts to do so result in pain and often convulsions

At times the patient seems to be perfectly normal and then again goes into a maniacal attack After two or three days of this the patient passes into a stage of exhaustion or a paralytic stage he is quiet and the convulsions cease He becomes unconscious often going into coma and the temperature rises to about 41 6° C (107° F) pulse is rapid the heart becomes weaker and finally death occurs

There is hyperemia and perivascular round cell infiltration of the central nervous system and congestion of the pharynx esophagus and stomach Typical and diagnostic Negri bodies are present especially in the ganglion cells of cerebral and cerebellar cortex

Diagnosis The animal should be obtained and subjected to an examination by a veterinary In case of doubt the animal is never killed but is observed for two weeks If rabid death occurs in four to six days Then the head is sent to a laboratory for an examination of the brain for Negri bodies It is a mistake to do away with the animal in the early stages of rabies since this results in failure to find the Negri bodies in the brain at examination

TREATMENT

Since death is inevitable treatment is purely palliative the object being to insure rest and control pain and convulsions

1 The patient should be isolated in a darkened quiet room and given sedatives as needed The ordinary sedatives have very little action in controlling the spasms but it is advisable to give morphine sulfate 0 016 to 0 032 Gm (¼ to ½ grain) hypodermically in an effort to diminish the severity of the spasms Chloroform inhalations to the point of coma are given Chloral hydrate 1 to 2 Gm (15 to 30 grains) avertin 60 to 80 mg (1 to 1⅓ grains) per kg or bromides 1 to 2 Gm (15 to 30 grains) may be given by rectum as indicated to prevent the distress of severe convulsive spasms

2 Local application of cocaine five per cent solution may relieve the sensitiveness of the throat so the patient may take liquid nourishment Administration of other foods is contraindicated and no foods or fluids should be given during the last stage of the disease although fluids may be administered by rectum during the last stage

3 Attendants should wear rubber gloves and take other precautions since this disease is highly infectious Dried saliva remains infectious for 14 hours while fluid saliva is infectious for twice that long

4 *Preventive treatment in rabies is most important because if it is not instituted a fatal outcome is almost certain*

a If a person has been bitten by an animal suspected of having rabies he should first be anesthetized so he may receive proper surgical care without pain

b Then the wound should be opened and blood forced out The wound should be cleansed with bichloride of mercury solution diluted 1 1000 or with a warm saline solution

c Fuming nitric acid or pure phenol should be used to cauterize the wound though another cautery may be used The nitric acid should be applied by drops to the torn surface especially to the deep punctures but care should be taken not to get the acid on bony or bloodless parts or on sound skin Carbolic acid may be used on these parts Some doctors object to the fuming nitric acid treatment because it may result in severe infections and scars

d Finally the wound should be washed with a saturated solution of bicarbonate of soda and then alcohol No attempt should be made to close the wound The dog should be saved for observation

e The *Pasteur* treatment for rabies is given as follows A series of inoculations of rabies virus is administered if there is any suspicion

that the wound was caused by a sick dog or one known to have rabies The dosage is 2 cc administered daily into the subcutaneous tissues in different areas for a period of about 21 days Care should be taken to give sufficient amounts of serum or it will be useless the amount of vaccine necessary is dependent on the location and severity of the bite It may be necessary to give 35 or 40 doses Because there may be an untoward reaction from the antirabies vaccination inoculations should not be given unless it is quite certain that the bite was from an animal with rabies Sections of the brain of the animal should be put in glycerin at the same time the original smears or sections are made and kept for either mouse or rabbit inoculation

f A recent suggestion for treatment is using immune transfusions in victims who have been severely bitten about the head Small blood transfusions from people who have recently completed a 21-day treatment by the Pasteur method are given

TRICHINOSIS

Trichinosis is an acute or subacute disease caused by the *Trichinella spiralis* It occurs wherever uncooked or improperly cooked pork is eaten and age sex race occupation location and climate appear to have no effect on the incidence The disease occurs most often during the summer months according to the author s experience probably because during this season the roadside stands selling hamburgers barbecues and homemade country sausage are open

Etiology Most patients reveal a history of having eaten raw hamburger or inadequately cooked pork The disease is produced by the Trichinella spiralis a slender roundworm developing from the encysted larval form in trichinous meat When a person ingests this meat the cyst wall is digested in the stomach and the worms pass into the small intestine where they reach maturity in about three days The females are fertilized and on about the seventh day burrow into the mucosa of the small intestines and allow the embryos to escape into the tissues and lymph spaces By the tenth day the embryos are usually found in the muscles where they grow to maturity they coil up and become completely encysted by the twelfth week and may live in this stage for 20 or 30 years

The development of trichinosis in humans is accidental but the lower animals are the normal hosts for the organism It is probable that swine become infected when their food contains uncooked pork

scraps The disease is not transmitted from person to person and humans do not appear to be immune after an attack

Signs and Symptoms Trichinosis does not always present a uni form clinical picture but the forms following the classic outline are usually easily recognized The incubation varies but symptoms begin 6 to 14 days after the ingestion of the trichinous pork in most cases However occasionally gastrointestinal disturbances commence a few hours after eating while in other instances characteristic symptoms may never appear The severity of the symptoms depends partly on the amount of infected meat eaten and on the number of parasites in the meat Other factors include the size physical condition and resistance of the individual and the amount of tissue invaded

The disease process may be divided into three stages

1 The stage of intestinal infestation occurs a few hours after the infected food is ingested The symptoms are referable to the gastro intestinal tract with loss of appetite nausea vomiting diarrhea and abdominal cramps There is a gradual rise of temperature prostra tion and some pain and stiffness in the muscles

2 The stage of dissemination begins about a week later when the embryos enter the blood and lymph stream Muscular pains are more pronounced and the function of the muscles especially those of respiration mastication and of the eye is disturbed Edema of the face and eyelids is common as are fever and profuse sweating Rash with tingling or itching of the skin may occur

3 The stage of encystment begins about the seventh week when the embryos become encysted in the muscles It is a period of con valescence in which the symptoms become less severe and gradually the temperature returns to normal and the edema subsides The pa tient is anemic and emaciated and the muscular pains and weakness may continue for months

Early in the disease the percentage of hemoglobin is moderately raised and the number of red blood cells may be increased Later anemia may develop with the number of red cells falling as low as 2 500 000 per cmm and the hemoglobin to 45 per cent Leukocyto sis usually about 25 000 white blood cells per cmm may be present The number of neutrophiles rises with the eosinophiles proportion ately increased This eosinophilia is one of the main characteristics of the disease but it is not always present Besides these clinical mani

festations which constitute the clinical picture of the typical case other less common signs and symptoms have been noted Fatigue generalized edema cough, headaches chills furuncles, hoarseness and marked hypotension may be present The electrocardiogram may confirm the clinical evidences of various degrees of temporary myocardial involvement Frequently trichinosis is complicated by the involvement of various organs with the presence of ocular neurologic or mental symptoms

Diagnosis The lack of a regular course and the many deviations from the clinical picture which are encountered may make the diagnosis somewhat difficult Usually the blood counts muscle biopsy and skin test are valuable diagnostic aids However a positive Widal reaction in the presence of persistent fever may suggest typhoid fever The muscle and joint pains may lead to a diagnosis of rheumatic fever or influenza and the rash and stiffness of the neck may confuse the physician as to whether the patient has trichinosis or meningitis Other conditions which may simulate trichinosis are acute nephritis tularemia sinus infection or la grippe

A history of having eaten hamburger sausage, ham or pork of any kind which may have been undercooked, an eosinophilia gastrointestinal disturbances generalized aches and fever are very suggestive of trichiniasis If there is any doubt a muscle biopsy often reveals larvae and makes the diagnosis certain Other diagnostic aids include the Bachman skin test in which the injection of trichinella protein causes a specific local skin reaction and the study of the blood for precipitins though this test is of little value before the twenty first day of the disease

Prognosis The immediate prognosis is good Few patients die and many cases are so mild that they go unrecognized However, the brain meninges kidneys and heart may be invaded and then the outlook is not so satisfactory Complications are usually limited to pneumonia pleurisy thromboses and thrombophlebitis

TREATMENT

Unless patients are seen before the larvae become encysted in the muscles or organs of the body only palliative treatment is of value However if the case is observed in the invasive stage a brisk cathartic as castor oil 15 to 3 cc or a saline purge as a solution of citrate

of magnesia 200 cc (1 bottle) followed in several hours by magnesium sulfate 10 to 15 Gm (150 to 225 grains) is very effective Good results have been reported in treatment with thymol dissolved in sterile olive oil 0 066 Gm (1 grain) in 1 cc of oil giving 2 to 3 cc subcutaneously or intramuscularly every day for seven days Sedatives as phenobarbital, 0 1 Gm (1½ grains) daily and acetylsalicylic acid 1 to 2 Gm (15 to 30 grains) three times a day may be administered to relieve the pain and headache To aid in the encystment of the larvae in the muscles after the invasive stage calcium lactate 1 Gm (15 grains) three times a day or some other calcium preparation may be given

The chief factor in treatment is the prevention which is accomplished by refraining from eating pork or pork products unless they are cooked properly

VINCENT S ANGINA

Vincent s angina is an ulceromembranous inflammation of the mucous membrane of the cheeks gums and fauces Its synonyms are ulcerative stomatitis fusospirillosis trench mouth and ulceromembranous angina

Etiology This rather common disease is found most often in young persons though it may occur at any age Poor health lesions of the mouth decayed teeth inflamed gums and oral uncleanliness predispose a person to this malady It is geographically widely distributed though it is seen most commonly in temperate or tropic climates where its incidence may be epidemic in character It spreads from person to person by kissing towels dishes or some such contact The disease may gain entrance through the ear vagina or glans penis

The two organisms associated with Vincent s angina are a fusiform bacillus and a spirochete which are found together in the lesions and most plentifully in the immediate vicinity of the ulcer They survive best in an acid medium

Pathology The inflammatory process is described as going through three stages (1) Hyperemia and edema (2) ulceration and (3) pseudomembrane formation with necrosis These stages are not however clearly separated from each other and may follow each other in rapid succession The lesion most commonly occurs on the gums cheeks pillars of the fauces tonsils and uvula though it may

appear on any of the other mucous membranes The mucous membrane of the female genitalia may become infected The organism may pass from the vulva through the vagina and involve the endometrium Noma gangrenous stomatitis and gangrene of the fauces are the most serious lesions Pulmonary involvement with bronchopneumonia and pulmonary abscess are also known to result from this disease These severe complications are most likely to come on if there is granulocytopenia

Signs and Symptoms Sore mouth and gums headaches general malaise chills fever and tachycardia are the symptoms associated with the disease Sometimes there are no constitutional symptoms only local pain on swallowing or tender gums hoarseness aphonia and paroxysmal cough No leukocytosis is present on the contrary there may be polymorphonuclear leukopenia This leukopenia probably is preexistent to the disorder and allows the infection to invade the mouth without much protective cellular response The spleen is not palpable

Ulcers are discovered in the mouth The ulcer may be single or the membrane may spread rapidly as in diphtheria In children the first sign may be painless enlargement of the cervical glands

The disease may be acute subacute or chronic with the lesions persisting for weeks or months Recurrence of such an attack is common

Diagnosis Diagnosis is confirmed by the presence of the typical Vincent s bacteria fusiform bacilli and spirilla Vincent s angina must be differentiated from syphilis diphtheria and tonsillitis

If a smear of the exudate is stained with carbolfuchsin and studied under the microscope there will be little trouble differentiating between Vincent s angina and diphtheria The fusospirillosis are found plentifully in Vincent s angina while they are absent in diphtheria Cultures will give further proof for the diagnosis The hyperemia surrounding the membrane is intense in diphtheria but not so marked in Vincent s angina In tonsillitis too the hyperemia is much greater than in Vincent s angina and the exudate is more punctate

A serious case of fusospirillosis with conspicuous edema is harder to diagnose as it is easy to confuse it with tonsillitis and diphtheria The bacteriology the necrotic character of the slough and the relatively mild surrounding hyperemia of fusospirillosis are the main dif

ferential points However it is well to remember that in tonsillitis there may be small numbers of the fusospirilla present and in the cryptic exudate of chronic tonsillitis this spirochete may be found in large numbers

The best way to differentiate syphilis is to examine a smear of the exudate *Spirocheta pallida* is very fine and shaped like a corkscrew while the other is coarser and has long undulating curves One should note that the fusospirillum often is found in syphilitics especially in those undergoing mercury therapy

Prognosis Vincent s angina is rarely fatal but may persist for weeks and recurrence is common Troublesome complications are rare The Vincent bacteria are more active in the presence of diphtheria bacilli than with streptococci The presence of pyorrhea decayed teeth or infected tonsils increase the severity of the attack

TREATMENT

Oral and dental cleanliness should be carefully maintained in all cases In order to avoid contaminating others towels and eating utensils should be kept separate After the attack is over local mouth disease and teeth may be attended to but operative work should not be performed until the Vincent bacteria are proved to be absent

The most satisfactory active treatment may be described as follows Hydrogen peroxide is applied to the lesion to remove the slough After that the lesion is washed thoroughly with saline solution and the ulcers dusted with arsphenamine If the gum margin is invaded arsphenamine can be best applied with a spray If the middle ear or nasopharynx is infected it should be cleaned according to the usual cleaning procedure and the ear canal carefully dried Arsphenamine is then blown into the middle ear

Glycerin 8 cc wine of ipecacuanha 12 cc and liquor potassii arsenitis 12 cc in combination are a good local application The solution may be diluted and used as a mouthwash There should be no granulocytopenia if arsenic is to be used If there is granulocytopenia every effort should be made to increase the granulocytosis

If the lesions are inaccessible arsphenamine can be given intravenously 0 3 to 0 6 Gm (4½ to 9 grains) for several doses at two or three-day intervals Novocain one per cent solution will relieve the cough due to severe laryngeal ulcerations and the dysphagia

Sulfadiazine is the most effective method of treatment at the present time It is given in doses of one gram every four hours until the sulfa level of the blood is approximately seven milligrams per cent then this level is maintained until the disease subsides Subsequently one gram once or twice a day is given for several weeks Corresponding amounts of soda bicarbonate are administered at the same time

LUDWIG S ANGINA

Ludwig s angina involves the cellular tissues of the floor of the mouth and sometimes the submaxillary space or tissues of the neck. It is a phlegmonous process resulting from infections within the floor of the mouth or from the teeth localizing in the floor of the mouth This disease is rare but virulent and often fatal

Etiology Ludwig s angina occurs most commonly in the young and young adults though no age is immune Males are more often attacked than females

Trauma of the interior of the mouth local mouth infections dental caries tonsillitis peritonsillitis trauma of dental extraction Vincent s angina facial erysipelas otitis media and externa and ulcers of the lip and nose are all said to cause Ludwig s angina at one time or another Infections of the tonsils and front teeth however are not likely causal factors

Streptococci staphylococci bacilla coli and sometimes gas producing organisms of the anaerobic type are found as a rule

Pathology Ludwig s angina is probably due to cellulitis though it has been attributed to lymphadenitis and a perilymphadenitis lymphadenitis would not cause a sublingual or submaxillary cellulitis unless there was direct extension of the infection to the cellular structures by contiguity

The sublingual space must be involved for a diagnosis of Ludwig s angina Infection may be above or below the mylohyoid muscles If above the abscess would point inside the mouth if below to the submental region

Signs and Symptoms In Ludwig s angina the first complaint is generally stiffness of the tongue and pain in the floor of the mouth and on clearing the throat A boardlike swelling of the submaxillary and submental regions with marked trismus is typical This swelling may extend to the clavicle in severe cases There is also swelling and

induration of the mouth gums and tongue, which is pushed back ward and upward Suppuration is not always present in such cases but abscess formation is evident in the majority of them The con stitutional symptoms resemble those of severe toxemia

Fever is not always present in the earlier stages but it may rise as high as 41 1° C (106 F) later on The leukocyte count may be from 10 000 to 35 000 or more Asphyxia may occur as a result of the swelling and displacement of the tongue

Prognosis The prognosis in Ludwig s angina is bad the mor tality may be as high as 43 per cent Death may result from suffoca tion or exhaustion Serious complications such as osteomyelitis of the mandible and involvement of the submaxillary the parotid or the pharyngomaxillary space may develop Jugular thrombosis may be brought on by invasion of the carotid sheath Mediastinitis is com mon If there is suppuration heart failure may come on rapidly

TREATMENT

Bed rest and a liquid diet are required The heart should be stimulated by caffein and digitalis Oxygen must be kept on hand ready for use

Surgical drainage of the pus should be effected Incisions below and parallel to the body of the mandible should be made and explora tion carried out with a blunt forceps Another vertical incision should be made above the hyoid bone to the lower border of the chin Some surgeons split the geniohyoglossus muscles apart by passing the me dian raphe of the mylohyoids with the object of relieving tension Hajek s clinic follows the procedure of making an incision along the anterior border of the sternocleidomastoid muscle and carrying out dissection with a blunt instrument or a sharp one if necessary as deep as the mucous membrane of the pharynx

If simple incisions fail the Mosher operation for parapharyngeal abscess may be performed If the condition is severe tracheotomy may be necessary and should not be delayed until the case is des perate

Hot fomentations consisting of ten per cent aqueous solution of ichthyol or of saturated solution of magnesium sulfate should be used as a supplement to surgical drainage

Convalescence which is always slow requires the use of tonics a liberal diet and an extended vacation

SEPTICEMIA

The commonest cause of septicemia is the streptococcus but it is often caused by other pyogenic organisms There is little difficulty in making the diagnosis especially if one takes advantage of laboratory facilities for blood cultures and other bacterial studies As a rule, a septic focus may be found which is responsible for the invasion of the blood stream

Signs and Symptoms An abrupt onset with chills and high fever is characteristic The chills follow no definite pattern as in malaria and the same may be said of the fever There may be generalized aches and pains and a thorough investigation of the chest, abdomen sinuses meninges and pelvis must be done As endocarditis is commonly associated with hemolytic streptococcus the heart is examined most carefully The neck is investigated for the stiffness of meningitis Palpation is done to determine if the spleen is enlarged The urine and the blood are examined and albuminuria red cells and pus cells are not uncommonly found in any case of septicemia Leukocytosis is the rule but leukopenia may be present There is always a decided increase in the band forms of polymorphonuclear leukocytes Blood cultures not one but many should be done as the first culture may fail to show the growth of organisms

TREATMENT

The course and prognosis of septicemia has been altered by the use of the sulfonamides and penicillin It matters little what organism causes septicemia the use of one of the sulfonamides is indicated and the following method is advocated The regular dose of one gram every four hours and the intravenous administration of 5 to 15 grams daily until the optimal sulfa level of 8 to 12 milligrams per cent is obtained

Penicillin with or without sulfa drugs is advocated in severe cases While there may be differences of opinion the commonly used method of administration is as follows 80 000 to 100 000 units are given intravenously in 1000 cc of normal saline solution and administered by the drip method Simultaneously, 10 000 units are given intramuscularly every four hours A response to this treatment is noted on the fourth or fifth day Unless there is a favorable

reaction by the fifth or sixth day of treatment the outcome is likely to be unfavorable

NOMA

Definition This is a form of microbic gangrene in and about the mouth and genitalia caused by a mixed infection generally with the *Spirocheta refrigens* and *Vincent s spirillum* Clinically it manifests itself as cancrum oris Ludwig s angina gangrenous balanitis and noma pudendi

(*a*) Cancrum oris is noma of the lips and gums It begins as a indurated red pimple on the mucous membrane (very commonly following an attack of measles) and this goes on to a sloughing ulcer and then to a wet gangrene which may involve the cheek jaws and whole side of face There is little pain but constitutional symptoms are severe *Mortality is about 70 per cent*

(*b*) Ludwig s angina (see page 398)

(*c*) Gangrenous balanitis is a spontaneous gangrene of the male genitalia occurring in middle aged individuals during or following an infectious fever There may be considerable tissue destruction but regeneration without deformity always occurs There is no mortality

(*d*) Noma pudenda is a moist gangrene of the vulva in children *which follows infectious fevers particularly measles Recovery* is usual

Treatment Intravenous arsphenamine is a specific in noma The nonresponsive case is treated as in cellulitis by free incision and drainage

CHAPTER XXI

Tropical Diseases

INTRODUCTION

The tropical diseases may be divided into groups on the basis of the mode of transmission namely by mosquitoes by direct contact with contaminated soil or water by ingestion of infected material and by lice or ticks

The mosquito borne group includes malaria dengue kala azar yellow fever filariasis and African trypanosomiasis The direct-contact group consists of hookworm disease and schistosomiasis The ingestion group consists of Weil s disease plague amebic dysentery bacillary dysentery cholera and ascariasis Those caused by lice or ticks are typhus endemic and epidemic relapsing fever Rocky Mountain spotted fever and American trypanosomiasis

Specific prophylactic measures for the diseases mentioned above will be considered in connection with the disease under consideration

MOSQUITO-BORNE GROUP

Prophylaxis General prophylactic measures such as destruction of adult mosquitoes by insecticides and aerosol pyretheum and control of mosquito breeding areas by covering stagnant collections of water with oil D D T and adequate drainage are prime factors in the elimination of these diseases The individual should be protected from mosquito bites by adequate screening of all buildings individual bed nets and spraying of living quarters with D D T for residual effect Head nets mosquito repellents and full length clothing should be worn in areas where infected mosquitoes are numerous Infected individuals should be treated in mosquito proof quarters

Malaria

Malaria is a specific infectious disease which is commonest in the tropical and subtropical regions where there is a heavy rainfall though it also occurs in more temperate climates Malaria has a

higher mortality rate and is responsible for more deaths per year than any other transmissable disease It is characterized by intermittent chills and fever recurring at regular intervals anemia and enlargement of the spleen

Etiology This disease is caused by the *Plasmodium malariae* (quartan parasite) the *Plasmodium vivax* (tertian parasite) *Plasmodium falciparum* (estivoautumnal parasite) and *Plasmodium ovale* (oval parasite) These are one-celled protozoa which are related but each has fundamental qualities which are peculiar to that one and each causes a certain type of malarial fever

Man is infected through the bite of the female Anopheles mosquito which has become infected by sucking the blood of a person with malaria

Asexual Cycle When the infected mosquito bites man sporozoites or spores (rod shaped parasites) are liberated into the blood stream Each of these spores penetrates a red blood cell becomes rounded and matures and initiates the stage of asexual development The red cell becomes pale and swollen and the parasite contains dark brown granules of pigment which it produces and later releases At maturity some become schizonts (asexual form) and some become gametocytes (sexual form) In asexual division the nuclear chromatin divides into fragments the cytoplasm separating so as to surround each of these These new bodies (merozoites) form a rosette within the periphery of the erythrocyte The rosette of merozoites breaks up at the end of a certain period of time (48 hours in tertian malaria 72 hours in the quartan type and variable in estivo-autumnal form) and these are discharged into the blood stream This occurs in all the infected red cells at about the same time and the sudden outpouring of foreign protein causes the chill fever and sweat of the malarial paroxysm In time gametocytes begin to develop in the peripheral circulation of the patient

Sexual Cycle The female mosquito sucks female macrogametes and male microgametes into her stomach when she bites a malarial patient These enter into a sexual union and form the zygote which penetrates the stomach mucosa producing an oöcyst The oocyst matures in 7 to 12 days depending on the species of plasmodium and bursts into the coelomic cavity dispensing thousands of fusiform sporozoites These migrate to the salivary glands and when the mos

quito again bites a human each sporozoite injected into the blood stream enters a red blood cell becomes amebulae divides into merozoites repeating the asexual schizogonic cycle

Signs and Symptoms Experimentally the incubation period may vary from 8 to 20 days though the time in humans is not known Paroxysms of chill fever and sweat are the main characteristics of malaria In the tertian type paroxysms occur every 48 hours every 72 hours in the quartan type and about every 24 to 48 hours in estivoautumnal malaria Other features include jaundice pain in the head back extremities and elsewhere vomiting and anorexia

The paroxysms are explained by the fact that the foreign protein or toxin which enters the blood stream when the infected red cells rupture suddenly causes a general relaxation of the entire vascular system Less blood flows through the capillaries and the surface of the body assumes the temperature of the surrounding air is cooled and the patient has a chill The fever continues until the toxin is neutralized when the sweat lowers the fever and eliminates the toxins

Pernicious malaria is usually fatal It occurs most often in the estivoautumnal type of the disease and is classified as follows

1 Cerebral form
   a Hyperpyrexia from involvement of heat center Temperature 110 F and up
   b Comatose onset with delirium without a typical rigor or after a typical onset This may develop
   c Epileptiform seizure due to cortical involvement
   d Psychic manifestations mania melancholia or delusional psychosis which may precede afebrile symptoms
2 Algid form characterized by collapse subnormal temperature weak and thready pulse and slow shallow respirations
3 Bilious remittant fever characterized by severe nausea and vomiting with jaundice appearing on the second day increasing for a few days and subsiding
4 Blackwater fever or hemoglobinuric fever is an allergic type The patient is sensitized to malarial toxins by repeated infections or insufficient treatment The attacks occur as a result either of a new infection usually with *Plasmodium falciparum* or the exacerbation of a latent infection by chilling intensive quinine therapy debility or concurrent disease
5 Cardiac bronchopneumonia types
6 Cachexia

Pathology In malaria the spleen and liver are most frequently involved In fatal cases the spleen is greatly enlarged smooth and ranges in color from gray to black because of pigment deposits The capsule is thin the pulp soft containing parasites pigment and other debris Microscopically the blood vessels are swollen and thick and often obstructed by large collections of parasites These parasites are found in the endothelial cells of the blood vessels and in the reticuloendothelial system too The liver is enlarged and congested with deposits of pigment The small vessels may be blocked and the endothelial and reticuloendothelial cells are gorged with parasites The kidneys brain bone marrow and vascular system are also congested

Diagnosis There is not much difficulty in making a diagnosis of acute malarial fever though in some cases the disease may resemble some other acute infectious disease as typhoid relapsing fever dengue and bacillary dysentery A definite diagnosis may be made after a study of the circulating blood using thick and thin smear technique or by sternal puncture A history of exposure of residence in a malarial district enlarged spleen or leukopenia and anemia should suggest the diagnosis If repeated blood smears are negative the subcutaneous injection of 0 5 to 1 cc of 1 1000 adrenalin may be followed by the appearance of plasmodia in the peripheral blood Four smears are made at 15 minute intervals following the injection If doubt still remains the quinine test may be done though it is not a definite aid If the fever persists after the administration of quinine the diagnosis of uncomplicated malaria is ruled out but the disappearance of fever does not make the diagnosis of malaria positive nor does it eliminate the possibility of another disease being present

Prognosis In the acute uncomplicated attacks of malaria of the tertian quartan or oval type recovery is almost certain Malignant tertian untreated carries a mortality of around 25 per cent

Relapses occur most frequently in the tertian type which is the most frequently encountered type of malaria These may be due to insufficient treatment and may be brought on by exposure fatigue overheating alcohol trauma other illness surgery and emotional upsets With the passage of time from highly endemic areas the frequency and severity of relapses from benign tertian shows an unmistakable trend toward the eradication of malaria within three years by development of immunity in the host

TREATMENT

1 **General Management**

a The patient should be protected so mosquitoes cannot bite him he should be kept in bed during the acute stage

b Fluids should be given only during the acute stage of the disease and when this has passed a light diet may be substituted Large quantities of fluids are necessary because of the fever and profuse sweating

c Hot water bottles and warm blankets should be applied to the patient during periods of chills

d After the chill when the temperature rises an ice pack should be placed on the head and tepid sponges given

2 **Specific Treatment** The National Research Council recommends the following procedure as the most effective treatment in malaria

a Atabrine 0 2 Gm (3 grains) and sodium bicarbonate 1 Gm (15 grains) by mouth with 200 to 300 cc of sweetened fruit juices tea or water repeated every 6 hours for five doses Thereafter 0 1 Gm (1½ grains) three times daily with meals for 6 days Total dosage 2 8 Gm in 7 days

b Quinine may be used in the presence of idiosyncrasy to atabrine or when atabrine is not available Quinine sulfate 1 Gm (15 grains) by mouth three times a day after meals for 2 days followed by 0 6 Gm (10 grains) three times a day after meals for 5 days Total dosage 15 Gm (225 grains) in 7 days

c The parenteral administration of atabrine and quinine should be restricted to the immediate treatment of the severe complications of falciparum malaria such as coma hyperpyrexia and the serious algid types or to any type of malaria complicated by vomiting of such degree as to render oral therapy impossible or ineffective

(1) *Intramuscular Atabrine* Atabrine dihydrochloride 0 2 Gm (3 grains) in 5 cc of sterile distilled water intramuscularly into each buttock If necessary one or two additional doses may be given at intervals of 6 to 8 hours Oral therapy should be instituted as early as practicable in such amounts as to give a total atabrine intake of 1 Gm in the first 48 hours Thereafter the dose should be 0 1 Gm (1½ grains) three times daily after meals for 5 days

(2) *Intravenous Quinine* Quinine dihydrochloride 0 6 Gm (10 grains) in 300 to 400 cc (minimum 200 cc) sterile physiologic saline solution injected intravenously and slowly During the injection indications of toxic effect—rising pulse rate and falling blood pressure—should be watched for This treatment may be

repeated in 6 to 8 hours if necessary It should be used in the presence of coma or hyperpyrexia and should be considered for the treatment of any falciparum infection in which 5 per cent or more of the red blood cells are parasitized

d Excellent results have been observed in a small series of cases with chloroquine and related compounds

Prophylaxis The following factors are important in prophylaxis against malaria

1 Prophylactic drug therapy using atabrine 0 1 Gm (1½ grains) daily has been found more effective with fewer side effects than quinine

2 Latent cases of malaria should be adequately treated as long as is necessary to prevent the spread of the disease

3 Measures outlined (p 428) for the control of mosquito vectors should be followed

Blackwater Fever

Blackwater fever is usually a complication of malignant tertian malaria often seen in persons residing in malarious zones for 12 months or more

Etiology The etiology is unknown though precipitating factors include fatigue alcoholism quinine trauma or chilling The disease is found in the same areas in which malignant tertian malaria is seen and is observed in its most severe form after chilling or repeated infections Those who have stayed in malarial districts a year or more and who have had repeated attacks of subtertian malaria are most apt to contract the disease and persons returning from malarial districts to cool or temperate climates may also be affected The condition may also be precipitated by active antimalarial therapy using plasmochin with quinine

Pathology The pathological changes are similar to those of malaria such as congestion of the kidneys congestive enlargement of the spleen and liver and hemosiderosis of the spleen liver and kidneys The gallbladder may be distended with thick blackish bile The bone marrow extending into the long bones may be hypertrophied

Signs and Symptoms Blackwater fever is preceded by enlargement of the spleen and liver associated with tenderness and by the passage of urine containing a great deal of albumin urobilin and detritus The incubation period is unknown and onset is sudden

Often the passing of black or red urine is an early symptom Chill prostration and sudden lysis of red cells mark the disease Hemoglobinuria fever and jaundice are the cardinal symptoms Jaundice appears within a few hours after onset and may become intensive if hemolysis is extensive or long continued The passage of hemoglobin leads to kidney irritation and acute nephritis and death frequently is due to anuria caused by precipitation of acid hematin in the tubules

Diagnosis *Diagnosis is based on the history and symptomatology The disease may be confused with yellow fever and bilious remittent malarial fever However in yellow fever the spleen is not enlarged and the jaundice comes on later The clinical manifestations of subtertian malaria are slower and the signs and symptoms less severe*

Prognosis This depends on the severity of the onset The mortality rate is from 10 to 60 per cent Anuria is an unfavorable sign The number of attacks influences prognosis and three attacks are usually fatal Complications include heart failure in the posthemolytic period severe anemia hyperpyrexia uncontrollable vomiting hiccough and sudden drop in temperature with prostration and coma

TREATMENT

1 Quinine and atabrine are contraindicated until convalescence is established

2 Complete bed rest and warmth are indicated The patient should not be moved

3 Alkalinization of the urine should be accomplished by giving large quantities of fluid (about 3000 cc daily) Sodium citrate and sodium bicarbonate are the best alkaline salts and may be given orally 0 6 Gm (10 grains) by mouth every one to two hours until the urine is alkaline and then in doses large enough to maintain alkalinity Intravenous sodium bicarbonate 0 5 per cent in five per cent glucose or glucose saline solution is good Hot saline enemas have been beneficial

4 Whole blood transfusions or washed packed erythrocytes should be used in the presence of a rapidly developing severe anemia

5 When convalescence is established if plasmodia are present in the blood 0 1 Gm (1½ grains) of atabrine should be given the

first day two doses of 0 1 Gm the second day and three doses of 0 1 Gm from the third to seventh days inclusive The patient should be carefully observed for recurrence of hemoglobinuria After recovery the patient should be removed from malarious districts for a year or more

Prophylaxis Individuals infected with malignant tertian or having a history of a previous bout of blackwater fever should remain out of highly endemic areas of malaria for a period of several years On returning prophylactic measures must be carefully carried out

Dengue

Dengue is an acute self limiting fever also known as dandy fever and breakbone fever transmitted by the Aedes mosquito and occurring in epidemic form It is usually nonfatal but extremely disabling during its course

Etiology Dengue is caused by a filtrable virus transmitted by the Aedes mosquito This disease occurs wherever the Aedes mosquito is found that is in almost any part of the tropical or subtropical world especially about the China Sea South Pacific Islands West Indies and the Mediterranean Dengue fever may occur in epidemics and moderately severe epidemics have occurred in the southeastern United States

Pathology Little is known concerning the pathology as fatalities are not the rule Inflammation of the brain lungs myocardium and kidneys has been seen The viscera particularly the liver may show cloudy swelling The liver may be fatty and there may be petechial hemorrhages in the gastrointestinal tract

Signs and Symptoms The symptomatology is extremely variable Typically this disease is ushered in by a sudden rise in temperature to 39 to 40 5° C (102 to 105° F) The face may appear congested and blotchy Headache and pains in the joints and back are prominent and there are also malaise prostration paresthesias and mental depression Dizziness soreness behind the eyes and pain on motion of the eyes are frequently present The pulse is slow in comparison to the temperature and leukopenia is present The lymph nodes may be enlarged

In a few days the fever drops to normal and remains so for several days Usually though not always it rises again and at this time a

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Pathology Little is known concerning the pathology as fatalities are not the rule Inflammation of the brain lungs myocardium and kidneys has been seen The viscera particularly the liver may show cloudy swelling The liver may be fatty and there may be petechial hemorrhages in the gastrointestinal tract

Signs and Symptoms The symptomatology is extremely variable Typically this disease is ushered in by a sudden rise in temperature to 39 to 40 5 C (102 to 105° F) The face may appear congested and blotchy Headache and pains in the joints and back are prominent and there are also malaise prostration paresthesias and mental depression Dizziness soreness behind the eyes and pain on motion of the eyes are frequently present The pulse is slow in comparison to the temperature and leukopenia is present The lymph nodes may be enlarged

In a few days the fever drops to normal and remains so for several days Usually though not always it rises again and at this time a

morbilliform rash appears on the backs of the hands and feet and spreads over the body Desquamation and pruritus follow

Diagnosis Influenza and yellow fever must be considered in the differential diagnosis The rash saddleback fever bradycardia leukopenia, geographic location and presence of Aedes mosquitoes are helpful in pointing out the true nature of the malady Dengue like fevers may confuse the diagnosis These fevers as Sandfly fever Panama six day fever seven day fever all resemble dengue but are milder and of shorter duration The recurring phase and rash are often absent

Prognosis Prognosis in uncomplicated cases is favorable

TREATMENT

Treatment is symptomatic Salicylates and codeine are effective

Kala Azar

Kala azar also known as dumdum fever tropical splenomegaly black sickness and splenic anemia of infants is a parasitic disease characterized by persistent fever splenomegaly chronicity and later hepatic enlargement anemia and leukopenia

Etiology Kala azar or visceral leishmaniasis is caused by a protozoan parasite *Leishmania donovani* and is transmitted by the sand fly *Phlebotomus* It is found in Asia Europe Africa and some areas of South America Man is believed to be the principal reservoir although in some areas infected dogs may be important

Pathology The chief lesion is marked hyperplasia of the reticulo endothelial system involving chiefly the liver and spleen The parasites multiply in these tissues causing destruction of the cells and the parasites in turn are taken up by other reticuloendothelial cells The splenic and hepatic enlargement are due primarily to the marked hyperplasia of the reticuloendothelial cells Similar changes take place in the bone marrow

Signs and Symptoms The incubation period ranges from 10 days to 6 months The onset may be abrupt or gradual usually with fever splenomegaly appears early There is no characteristic febrile course As the disease progresses marked emaciation appears drenching night sweats are common Later in the course of the disease a gray color of the skin occurs from which the synonym black disease

is derived This is chiefly noted on the hands nails and forehead Anemia and leukopenia develop as involvement of the reticulo endothelial system takes place Alteration of the plasma proteins with a marked increase in the serum globulins occurs early The total protein is markedly increased with the most pronounced changes being in the globulin fraction In very severe cases wasting of tissue is marked chiefly in the extremities Edema of the extremities and ascites result from the marked alteration of blood proteins

Diagnosis In endemic areas the diagnosis can usually be made on the basis of splenomegaly hepatomegaly anemia leukopenia fever and alteration of the blood proteins Definite diagnosis can only be made on the demonstration of *Leishmania donovani* in the blood or other tissues The parasites can usually be demonstrated in un treated cases in the leukocytes and monocytes of peripheral blood Sternal puncture and splenic puncture are frequently of value when peripheral blood smears are negative

Prognosis Prior to the introduction of antimony therapy mor tality ranged from 40 to 90 per cent at present it ranges from 2 to 7 per cent in adequately treated individuals

TREATMENT

Patients who are severely ill must be kept at bed rest and treated symptomatically Neostibosan is the drug of choice and is adminis tered intravenously in a 5 per cent solution for adults giving 0 2 Gm initially followed by 0 3 Gm daily for eight to twelve doses Careful attention should be paid to untoward reactions from this drug

Tartrates of antimony were formerly used extensively but are being replaced by newer preparations Stilbamidine is the most powerfully known drug for the treatment of kala azar and has been used in refractory cases

Prophylaxis Avoidance of areas where the disease is endemic and protection against bites of the sand fly by the use of full length clothing and mosquito repellants are of value

Yellow Fever

Yellow fever is an acute infectious disease due to a specific fil terable virus which is transmitted by *Aedes aegypti* mosquitoes It is confined more or less to certain geographical areas especially South

America and West Africa where it is endemic From these points it may spread in epidemic form to other localities but fortunately the disease does not seem to become a permanent fixture there It prospers especially in low country with a warm damp climate where conditions for mosquito propagation are favorable Yellow fever runs an acute febrile course with remission on the third or fourth day and is characterized by jaundice hemorrhages and albuminuria No specific treatment has been found satisfactory but prophylaxis has brightened the outlook somewhat

Etiology Yellow fever is transmitted by the female mosquito *Aedes aegypti*, which sucks blood from a patient during the first three or four days of the disease By the fifth day the virus disappears from the blood stream and antibodies develop Ten or twelve days later the mosquito becomes infective and may transmit the infection to a susceptible person through its bite However it takes from four to six days for the disease to develop in nonimmune people Thus almost three weeks elapse between the appearance of the first case in a community and other cases

Pathology General features noted at autopsy include jaundice and evidence of hemorrhage in the stomach intestines gallbladder, meninges pleura pericardium and epicardium uterus lungs and bladder The most striking changes are in the liver kidneys and heart The liver is pale yellow and fatty the kidneys are tense and swollen and the heart is pale and flabby Microscopically the lesions consist of fatty degeneration and necrosis of the parenchyma with practically no inflammatory reaction and other degenerative changes

Signs and Symptoms The incubation period is usually from four to six days The initial stage of the disease is characterized by sudden chilliness or rigor severe frontal headache and general muscular pains especially in the back and limbs The general picture is one of intoxication rather than infection The temperature rises to 38 3 to 40° C (101° to 104° F) or more within 24 hours the face becomes flushed and bloated and the conjunctivae injected and red There is loss of appetite with nausea and occasionally vomiting Albuminuria is present and there may be slight jaundice The tongue is red and clean along the edges and tip with coating of the dorsal surface The pulse while remaining full and strong becomes slower and slower as the temperature rises after about 24 hours the

fever begins to drop but not as quickly nor consistently as the pulse rate This pulse fever symptom is one of the characteristic signs of the disease During this period the patient presents a picture of active congestion with severe prostration At the end of 48 to 72 hours these symptoms decline and a period of remission marks the end of the infectious stage This gives the false impression that the case is a mild one but within a few to 24 hours more specific manifestations appear

During this second stage vomiting becomes severe and has the appearance of coffee grounds the temperature rises to 39 5 C (103 F) or higher followed by intense thirst and gastrointestinal hemorrhages are severe Large amounts of albumin are present in the urine which is scanty in amount there may be complete suppression which if persistent causes death Venous congestion with low arterial tension takes the place of the active congestion of the infective period The spleen is not enlarged The conjunctivae are injected and jaundiced and the sclerae are also jaundiced as is most of the body Jaundice ranging in color from lemon yellow to a deep brown hemorrhages and consequent black vomit and albuminuria are the main features of this phase of the disease

The sixth or seventh day of the disease usually marks the turning point the patients either die then or the temperature rapidly falls by lysis The occurrence of anuria is a bad omen because it indicates liver destruction One of the most favorable prognostic signs in a severe case is the restoration of renal function The period of convalescence is from two to four weeks with complete restoration of kidney and liver function

Diagnosis Yellow fever must be distinguished from malaria and relapsing fever by blood smears In general the chief clinical manifestations of jaundice bradycardia leukopenia and hyperpyrexia in a yellow fever area make the problem of diagnosis an easy one However mild cases or those seen in the early stage may present some diagnostic difficulty

Dengue in its early stage must be considered when making a diagnosis but in this disease the spleen is enlarged and after two or three days the characteristic eruption appears Jaundice or hemorrhage is not present in dengue Weil s disease and infectious hepatitis may offer the most difficulty in differential diagnosis since the symptom

complex is almost the same as in yellow fever However inoculation of the guinea pig with blood or urine from the patient and consequent development of Weil s disease makes the diagnosis evident

Prognosis *In epidemics the mortality may be as high as 50 per cent* among the native population the mortality is about 7 per cent

TREATMENT

Yellow fever is a disease of uncertain prognosis since there is no specific therapy of definite value Consequently treatment is symptomatic with careful nursing

1 Since the circulatory mechanism is involved absolute bed rest in the recumbent position is important The patient should not be moved particularly not after the first day Movement is not only *hazardous but may aggravate the nephritis*

2 A saline purge as magnesium sulfate 10 to 15 Gm (150 to 225 grains) should be given on the first day and enemas daily thereafter

3 Foods should be withheld during the first stage of the disease and until the temperature returns to normal Water and citrus fruit juices should be given frequently in small amounts If vomiting prevents the ingestion of fluids intravenous dextrose 2000 to 3000 cc of a five per cent solution daily physiologic solution of sodium chloride 2000 cc by hypodermoclysis daily and tap water by rectum should be administered

4 Vomiting may be relieved by cracked ice and cocaine hydrochloride *0 016 Gm (¼ grain) by mouth* and *codeine* sulfate 0 033 Gm (½ grain) hypodermically

5 Headache and fever may be relieved by ice caps and sponge baths

6 Stimulants are not usually necessary early in the disease but they may be used later when collapse or asthenia develop

7 Hot baths or hot packs and cups applied to the loin may be of value if there is suppression of urine

Prophylaxis Specific vaccination confers an immunity and effective protection of several years duration

Filariasis

Filariasis is an infection of the lymphatic and connective tissues of man with nematode worms of the genus Wuchereria It is trans

mitted from man to man by mosquito causing lymphangitis and lymphadenitis with later development of localized edema

Etiology The most common species is *W bancrofti* found in most of the tropical world and in a small district of South Carolina The filaria develop in the mosquito and are passed to man by the bite of the infected mosquito which enables them to penetrate the skin The development of larval forms of *W bancrofti* has been shown to occur in 30 species of mosquito including Anopheles Culex Aedes and Mansonia types There is a latent period of about one year between time of exposure and development of symptoms

Pathology The essential pathological change in filariasis is an inflammatory reaction followed by obstruction of lymphatic channels by scar tissues These changes occur in the vicinity of adult worms Common sites are tissues of the external genitalia mammary glands lymph nodes of the extremities and superficial structures Chronic lymphatic obstruction and fibrosis lead to thickening of the skin and subcutaneous tissue and the development of elephantiasis

Signs and Symptoms Neurasthenic symptoms predominate early anorexia lack of energy constant fatigue headache drowsiness and photophobia Local swellings and lymphangitis appear early fever and chills are uncommon Lymphadenitis is most marked proximal to the involved areas Leukocytosis is present in about one third of cases and eosinophilia in about two-thirds

Physical findings described above may develop quickly and disappear in a similar fashion Repeated infections cause permanent enlargement and thickening of the areas distal to the involved lymphatic tissue Exacerbations are caused by trauma intercurrent infection and excessive exercise

Diagnosis A history of exposure to the disease in an area where it is known to be endemic a prolonged incubation period between time of exposure and development of first signs and symptoms and a series of recurrent attacks usually brought on by sudden exercise or strain are essential for diagnosis Objective findings of swelling of an extremity or of the scrotal contents and lymphadenopathy are necessary There is no specific laboratory test that is generally applicable and reliable for the diagnosis of this disease Microfilariae may be demonstrable in the peripheral blood early in the course of the disease Adult worms may be present in affected lymph nodes

but biopsy is contraindicated because it predisposes to further lymphatic obstruction

Prognosis Mortality in this disease is very low and elephantiasis and persistent edema result only from multiple filarial infections

TREATMENT

No drug is known to be specific for filarial infection and none will destroy the parasites during the life of the human host During acute attacks the patient should be kept at bed rest compresses should be applied to local inflamed areas Sulfadiazine may help to control secondary infections in elephantiasis Reassurance of patients is extremely important in this disease

Prophylaxis Prevention of the disease depends upon segregation of individuals from infected native populations and control of mosquito vectors

African Trypanosomiasis

African trypanosomiasis commonly known as sleeping sickness is a specific parasitic infection characterized by fever weakness wasting and protracted lethargy

Etiology The etiological agents are *Trypanosoma gambiense* and *Trypanosoma rhodesiense* They are transmitted by the tsetse fly genus Glossina The trypanosomes are blood parasites found in man and also in some wild and domestic animals which may serve as reservoirs for the disease

Pathology There is chronic inflammation of the lymphatics due to the mechanical action of the parasites or their toxins and the glands become enlarged The lymphatics of the brain and spinal cord are also concerned in this process Meningoencephalitis meningomyelitis proliferation of the neuroglial elements and lymphocytes and the endothelial cells about the perivascular lymph spaces follows the fever in the early stage The changes are most prominent about the vessels of the pons and medulla This leads to malnutrition cerebral changes and sleepiness Adenitis may be seen on gross examination in the neck groin and other lymph glands The cerebrospinal fluid is increased often turbid and the dura mater may be adherent in places The pia mater frequently is thickened in some parts The brain is congested as is the cord and hemorrhages in the cord are not uncommon There may be ascites and excess pericardial fluid

Pneumonic changes sometimes occur in the lungs and the spleen is enlarged Gross lesions of the brain and other organs may not be visible Trypanosomes are present in the cerebrospinal fluid lymph channels and blood

Signs and Symptoms The bite of an infected fly results in more marked inflammation than that of an uninfected fly There is an incubation period of ten days to three weeks followed by irregular remittent fever rapid pulse deep hyperesthesia and asthenia Head aches and neuralgic pains are associated with these symptoms In the rhodesian type delirium and high fever may set in early Whites who are suffering from this sickness have a characteristic erythematous rash on the trunk or thighs and the skin is often dry Hepatomegaly and splenomegaly may occur and the Wassermann reaction is some times positive Lymphadenopathy of the posterior cervical triangle is very characteristic The cerebral stage starts in with tremors of the tongue and fingers headache hysteria mania delusions and a desire to sleep Wasting is prominent as the disease progresses When the disease is far advanced recovery is rare

Diagnosis The clinical diagnosis is established if trypanosomes can be demonstrated in the blood spinal fluid or material obtained by cisternal or lymph gland puncture Thick dry blood smears or fresh wet preparations are of aid If organisms are not present on mi croscopic examination monkey dog guinea pig or white rat inocula tion may reveal them Repeated blood examinations are necessary and the absence of trypanosomes does not exclude sleeping sickness

The positive Wassermann reaction fever enlarged glands and erythematous rash may suggest syphilis and the increase of mononu clear cells may cause confusion with malaria syphilis and kala azar

Prognosis Mortality of this disease ranges from 5 to 90 per cent in various sections with a morbidity of 10 to 15 per cent

TREATMENT

1 Early cases of the gambian type may be treated with trypars amide dissolved in 10 cc of distilled water (not salt solution) Fifteen injections are given at weekly intervals The initial adult dose is 1 0 to 1 5 Gm (15 to 22½ grains) and subsequent doses are from 2 to 3 Gm (30 to 45 grains) Treatment should be rigorous so as to avoid arsenic fastness This drug may cause optic atrophy The dose

should be reduced and the intervals between injections increased if photophobia lacrimation eye pain, or dimming vision occur

If tryparsamide is not tolerated, give naphuride (Winthrop) (Bayer 205, antrypol) intravenously 10 cc in distilled water, every four days for four to six doses The initial adult dose is 0 3 to 0 5 Gm (4½ to 7½ grains) followed by injections of 1 Gm (15 grains) This drug is a kidney irritant and should not be used if albuminuria is present If albuminuria develops during treatment the drug should be stopped

Before and after completion of treatment lumbar puncture must always be made A case should be kept under observation for two years Examination of centrifuged citrated blood every month for three months after treatment is indicated and blood examinations should then be done every six months for two years

2 The rhodesian type does not respond to tryparsamide so therapy is started with naphuride as given for the gambian sleeping sickness Lumbar puncture and follow up studies are also required in these cases

3 Late cases are benefited only by tryparsamide as given for the early stages The drug should not be given intrathecally and the first dose should be half the standard dose Twenty weekly injections are given and repeated after a one to three month rest period The spinal fluid examination is a guide to therapy and should be studied before and after the second course of treatment and also six months and one year later More advanced cases need to be followed for three years

4 Patients should be segregated and kept in screened rooms

Prophylaxis Infected persons should be examined and treated before being allowed to go to districts where the tsetse fly is prevalent Measures should be taken to provide protection from the bites of the tsetse fly Chemoprophylaxis with naphuride 1 0 Gm (15 grains) in one injection every three months is desirable

DIRECT-CONTACT GROUP

Prophylaxis In that the prophylaxis for the two diseases in this group is individual it will be mentioned after the discussion of each disease

Hookworm Disease

Hookworm disease is a parasitic infection of the small intestines causing tissue destruction and blood loss in proportion to the severity of the infection The disease is prevalent in the southern United States and humid tropical regions being most prevalent in areas with poor sanitation

Etiology Etiologic agents are the *Necator americanus* in the Western Hemisphere and *Ancylostoma duodenale* and *Necator* in the Eastern Hemisphere Dog hookworms *Ancylostoma braziliense* and *A caninum* in the larval stage can infect the skin of man and cause creeping eruption The eggs are passed from an infected individual in the feces and hatch rapidly in the soil into the larval or filariform stage The parasite infects man in the filariform form passing through the skin up through the lungs up the respiratory tract over the epiglottis and down to the small intestine where it becomes attached When sexually mature oviposition occurs The Negro race is not so much affected as the white race

Pathology The site of entrance shows a dermatitis The lesion consists of a serpiginous tunnel into the stratum germinativum which may be followed by creeping eruption The larvae in the lung may cause hemorrhages Anemia is the rule and in severe cases ankle edema occurs Where the worms are attached in the intestines there may be small punctate hemorrhagic spots or larger hemorrhages Older hemorrhages are marked by punctiform pigmentation The heart may be dilated and the muscle may be flabby and show fatty degeneration The liver and kidney also show fatty changes and the spleen is often small The presence of grains of yellow pigment giving reactions of haematoidin in the liver and kidney suggests that there is intravascular blood destruction in which hemolysis is a factor

Signs and Symptoms An early symptom is dermatitis occurring chiefly about the toes or inner side of the soles of the feet but this is not a necessary part of the syndrome Mild infestations are asymptomatic and the chief symptoms are those of anemia with weakness palpitation and asthenia With more severe infection epigastric distress episodes of acid eructation exertional dyspnea headache and vertigo may be present and with more severe chronic infections ankle edema dilatation of the stomach and a protruberant abdomen may occur More marked findings are common in younger individ

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tails Patients are both mentally and physically sluggish Severe anemia is characteristic There is eosinophilia and sometimes leukocytosis

Diagnosis Diagnosis is established by the finding of characteristic eggs in the feces Beriberi chronic nephritis malarial cachexia and Ascaris infections must not be confused

Prognosis Prognosis is most serious in young children as their mental and physical development is retarded The outlook is serious in pregnant women and better in Negroes than in whites Treatment is usually successful unless the patient is debilitated by another disease or has a tendency to pernicious anemia Life expectancy is shorter in those who have hookworm disease since it renders them more susceptible to other diseases The mortality rate for hookworm disease itself has been quoted at from one to seven per cent

TREATMENT

1 The worms must be expulsed by the use of tetrachlorethylene in the absence of Ascaris infection The adult dose is 3 cc in a hard gelatin capsule followed in two hours by a saline purge If Ascaris infection is present give hexylresorcinol crystoids (caprokol) 1 Gm (15 grains) Food should be avoided for four hours after treatment This medication results in the killing of all the Ascaris infection and about half of the hookworm infection It should be followed in three days by treatment with tetrachlorethylene in order to eradicate all the hookworms These drugs have no serious toxic effects A light meal free from fat should be eaten the night before and the drug given on an empty stomach

2 If anemia is present iron is needed and ferrous sulfate capsules (exsiccated) 0 35 Gm (5 grains) t i d after meals are suitable

3 The diet should be high in iron and vitamins

4 One week after drug treatment the stools should be examined and if eggs are still found treatment should be repeated until the patient is cured

5 The creeping eruption may be relieved by soaking cotton in ethyl acetate applying it to an area just a little larger than the skin lesion and covering it with adhesive tape for 24 hours Or an area up to one inch beyond the edge of the lesion should be frozen with ethyl chloride spray or dry ice

Prophylaxis In heavily infected areas it is necessary to carry on mass treatment of the population to eliminate the source of infection This should be followed by an educational program to instruct the people on the mode of spread of the infection Shoes should be worn in all areas which may have been contaminated by native excreta

Schistosomiasis

Schistosomiasis is a parasitic infestation of man caused by flukes of the genus *Schistosoma* which live in the portal vein and its branches

Etiology Three etiological agents are responsible for varieties of this disease *Schistosoma haematobium* which causes genitourinary symptoms is found chiefly in Africa the *Schistosoma mansoni*, caus ing intestinal symptoms is likewise found in Africa and the *S japonicum* which brings on liver disturbances is more common in the Orient

The *Schistosoma* eggs hatch out shortly after being passed and the larvae liberated infect certain species of snails These snails are apt to be found in fresh water streams irrigation ditches reservoirs small pools and such places The larvae emerge from the snail into the water and infect man or animals by way of the skin The eggs of *S haematobium* are passed in the urine and those of *S mansoni* and *S japonicum* in the feces

Pathology Minute petechiae may be seen at the site of invasion of the parasite through the blood vessel wall Some days later there may be a urticarial rash The blood often shows a leukocytosis and eosino philia early Hepatic and splenic enlargement are marked especially in *S mansoni* and *S japonicum* infections Later in the course of the disease marked local inflammatory reaction followed by fibrosis is found in the bladder in *S haematobium* infections and in the bowel liver and spleen in *S mansoni* and *S japonicum* infections

Signs and Symptoms The chief sign of *Schistosoma* infection is papular dermatitis at the site of penetration of the skin by the para site There may be a latent period from 3 months to 2 years from the time of infection to the development of further symptoms In *S haematobium* infection terminal hematuria is an early symptom followed by frequency and burning on urination Splenomegaly and severe anemia are characteristic of *S mansoni* infection Irregular fever hepatic enlargement vomiting and hematemesis are frequently

nals Patients are both mentally and physically sluggish Severe anemia is characteristic There is eosinophilia and sometimes leukocytosis

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sive dose is increased by 1 25 cc until 7 5 cc are being given The course of therapy should include from 12 to 15 doses until 360 cc total or 0 648 Gm of antimony have been given This drug should be administered two or three hours after a light meal and the patient should rest for one hour after treatment Toxicity is an indication for reduced dosage Toxic symptoms may include coughing immediately after administration nausea vomiting dizziness and collapse The drug is contraindicated in cases with jaundice nephritis or severe hepatic disease It should be slowly injected into the lumen of a vein as thrombosis may occur otherwise It should not be introduced to the subcutaneous tissues as it causes necrosis

3 The use of emetine 0 6 Gm (9 grains) for ten injections has been followed by good results The first two injections should be 0 03 Gm (½ grain) and the rest 0 06 Gm (1 grain)

4 The diet should be liberal and nourishing If liver damage is present it should be high in carbohydrate and low in protein Supplementary vitamins especially vitamins A and B are good

5 The treatment of the local conditions is necessary and the urinary calculi growths in the bladder cystitis occurring in *S haematobium* infections may require surgical procedures Ascites which may develop in *S mansoni* and *japonicum* infestation may need to be tapped Splenectomy has been done for the splenomegaly but great care should be taken in selecting patients

Prophylaxis Bathing washing swimming laundering clothes and drinking of fresh water in endemic areas must be controlled If one accidentally touches such water one should immediately bathe completely with soap and clean water Water for drinking or preparation of food should be adequately chlorinated or boiled prior to use

seen With S *japonicum* infection profuse dysentery with fever occurs early Later fever with anemia leukopenia shrinking of liver and spleen with the development of ascites edema of the extremities and exacerbation of dysentery occurs Exhaustion or terminal infections usually cause death

Diagnosis *S haematobium is diagnosed by the finding of* characteristic terminal spined ova in the urine This type of Schistosoma egg is seldom found in the feces The ova of the *S mansoni* are lateral spined and occur usually in the feces *S japonicum* ova are spineless though a rudimentary lateral spine may sometimes be seen and are found only in the feces Characteristic lesions are seen in the bladder wall on cystoscopic examination and in the rectal wall on proctoscopic and can be confirmed by a microscopic examination of a biopsied lesion

Prognosis Prognosis depends on the intensity of the infection Mild cases may not result in great inconvenience but severe ones may be followed by chronic cystitis calculi renal disease and malignant growths The use of antimony has improved prognosis

The outlook in S mansoni infections is fairly good if the disease is mild and treated in time but bad in the presence of cirrhosis or *splenomegaly accompanied by ascites In these instances the disease* becomes chronic but the patient may live for years Intestinal ulceration dysentery and extensive papillomata of the rectum are unfavorable signs Infection with *S japonicum* is most serious and treatment is ineffective unless started early before visceral lesions are advanced Exhaustion or terminal infection usually cause death

TREATMENT

1 The worms may be expelled by the use of fuadin (neoantimosan *6 3 per cent solution of a trivalent organic* antimony compound) intramuscularly On successive days 1 5 cc 3 5 cc and 5 0 cc are given and then 5 0 cc on alternate days for ten doses In the presence of toxicity such as vomiting or joint pain the dosage should be reduced If eggs are present after treatment repeat this medication after 2 weeks rest for the patient

2 If fuadin is not beneficial give potassium antimony tartrate (USP) two per cent freshly prepared solution intravenously on alternate days The dose is initially 2 5 cc (0 05 Gm) and each succes

which is found in some rats The urine excreted by the rats contains the organisms and thus the disease is transmitted to man most commonly by contamination of water and rarely by some insect or through the soil abrasions in the skin nasal passages mucous membrane of the conjunctivae of the eye, or gastrointestinal tract The disease occurs most often in young adult males particularly soldiers in the trenches miners fish cleaners and others exposed to dampness or rat infested areas It is found the world over especially during the summer months

Pathology Most cases reveal generalized jaundice and lesions of the kidneys liver capillaries, and skeletal muscles The kidneys are enlarged jaundiced and swollen with rather marked necrosis of the epithelium of the convoluted tubules and interstitial infiltration of the lymphocytes and polymorphonuclear leukocytes Renal damage is almost entirely tubular ranging from cloudy swelling to necrosis

The liver is usually enlarged and bile stained Microscopically there is proliferation of the hepatic cells evidence of degeneration and inflammation as necrosis and dissociation of cells and signs of biliary stasis in the central part of the lobule Hemorrhages either slight or profound appear throughout the body especially in the peritoneum and pleura kidneys brain and meninges nasal mucosa skin adrenals and gastrointestinal tract The muscles of the calf are most frequently and extensively affected though the pectorals back muscles and deltoids are often involved Many other pathological changes are found but are not constant manifestations of the disease The spirochetes are most easily demonstrated in the kidneys and liver though they are also found in the myocardium adrenals skeletal muscle intestinal wall and other organs

Signs and Symptoms In general Weil s disease is divided into three stages (1) The febrile or septicemic (2) the icteric and (3) the convalescent period

1 *The Febrile Stage* The onset of the disease is sudden following an incubation period of from five to seven days There is usually a severe frontal headache with chilly sensations and severe prostration Muscular aching is marked and there is tenderness to slight pressure over the calves of the legs Anorexia nausea and vomiting and diarrhea are common symptoms Physical examination reveals

CHAPTER XXII

Tropical Diseases

(Continued)

INGESTION GROUP

Prophylaxis In prophylaxis for the gastrointestinal or ingestion group serious attention must be directed to see that water used for cooking and drinking is from a known pure source and not contaminated by excreta from animals or humans All water of questioned purity should be chlorinated or preferably boiled or distilled before use

All vegetables eaten raw should be thoroughly cleaned with sodium hypochloride This is particularly true in areas where night soil is used for fertilization All help engaged in the preparation of food should be carefully examined for the presence of a parasitic infestation and treated thoroughly

Patients under treatment should be strictly isolated in a screened room Linens and other materials contaminated by the patient should be sterilized or disinfected Individual utensils as thermometers and toilet articles for each patient is advisable Attendants should wear gowns when in contact with patients and should scrub thoroughly on leaving infected quarters Visitors should be limited and they must observe the same precautions required of attendants Patients should not be discharged until they have had repeated negative stool examinations

Weil s Disease

Weil s disease or acute spirochetal jaundice as it is sometimes called is an acute specific infection caused by the *Leptospira ictero hemorrhagiae* It may be either endemic or epidemic in character but it is more often the latter The disease is characterized by sudden onset with profound prostration muscular pain high fever jaundice and hemorrhagic tendency but these are not all necessarily present

Etiology The *Leptospira icterohemorrhagiae* produces Weil s disease It is a poorly formed spiral spirochete with hooklike ends

ure hemorrhage severe toxemia or complications as pneumonia myocarditis or vegetative endocarditis

At the end of the second week the patient becomes rational diuresis takes place jaundice subsides and the blood urea nitrogen begins to fall About this time the blood becomes sterile and the organisms appear in the urine During this period of leptospiruria specific antibodies appear in the blood and by the end of the third week very high agglutinin and lysin titers are demonstrable

3 *The Convalescent or Final Stage* After two or three weeks the third and last phase sets in The icterus index starts to fall and renal disease if present disappears Fever and hemorrhagic tendency are usually absent by this time and the patient is symptom free except for marked weakness Convalescence is usually uneventful lasting from a week or two to ten weeks Relapses may occur during the third to fifth weeks of the disease but are seldom of serious consequence Complications noted include peripheral neuritis leptospiral vegetative endocarditis or iridocyclitis

Diagnosis Weil s disease is easily overlooked in cases where jaundice is absent or hemorrhagic tendency slight A history of contact with rats or with a sick animal is suggestive The presence of the classical symptoms of sudden onset high fever severe headache muscular pains albuminuria and urea retention should make one think of Weil s disease However the causative organism must be found before a final diagnosis can be made

The *Leptospira icterohemorrhagiae* is circulating in the blood during the first week and a dark field examination or inoculation of a young guinea pig with blood intraperitoneally thus reproducing the disease are helpful diagnostic methods The first test is the simplest and most useful the latter is of no clinical significance since the patient will recover or die before the disease occurs in the pig The organism is from 8 to 15 micra in length and appears as an actively motile rapidly spinning spirochete It is tightly coiled with a small sharp hook at each end so it resembles the letter S During the second week the organism is excreted in the urine A dark field study of the urine is of little value but inoculation of a guinea pig may be of aid The agglutination test is probably the one of choice Usually this test is positive at the beginning of the third week and remains so for six months to a year Occasionally specific antibodies

in acutely ill patient with a high fever of 39° to 41 1° C (102 to 106 F) a full fast pulse hot dry skin red, puffy face injected conjunctivae dry coated tongue, injected pharynx and evidence of capillary damage may manifest itself as petechial and ecchymotic hemorrhages over the entire body Stools are usually light in color and bile stained urine is dark, scanty in amount and of high specific gravity frequently containing casts albumin bile pigment and red blood cells The liver is usually enlarged and tender the upper ab domen is tender and the spleen enlarged Leukocytosis is present from onset and at times there is an eosinophilia Red blood cells platelets and hemoglobin may be reduced Signs and symptoms in crease in severity during this period The leptospirae are found in the blood and a diagnosis may be made by dark field examination lysis agglutination test or by injecting blood from the patient into a guinea pig and thereby reproducing the disease On about the fifth day antibodies appear in the blood and by the tenth day the lepto spirae have disappeared

2 *The Icteric or Second Phase* This occurs from three to nine days after the onset of the disease Jaundice begins and increases rapidly and the hemorrhagic tendency becomes more apparent Evi dences of renal failure manifest themselves during this period there may be marked oliguria occasionally anuria increased urea reten tion and renal acidosis The temperature fluctuates toward the end of the first week and is usually near normal with a relatively high pulse rate at this time Headache and vomiting disappear

The patient is semicomatose and extremely toxic Although from the temperature chart one might conclude that the patient was recov ering examination shows that he is worse instead of better The liver is enlarged and sometimes tender There is often moderate abdomi nal distention peristalsis is diminished The spleen is not palpable Muscle tenderness of the back and calves is evident and tendon re flexes are diminished A rash may appear A high and rising icterus index and blood urea nitrogen are noted The white count may remain constant or rise to leukemic levels while the red count may decrease somewhat Urine is still scanty deeply colored with in creased amounts of albumin casts cellular débris and bile pigment In fatal cases death usually occurs between the ninth and sixteenth day It may be due to renal or cardiac failure renal and hepatic fail

c Barbiturates are indicated for sedation cardiac drugs for myocardial weakness and oxygen for pulmonary edema

2 The therapy of choice is the use of penicillin in large dosage and of immune serum in full doses of 30 to 60 cc in the early course of the disease

3 Arsenicals have not been proved of definite value Fair results have been obtained with bismuth subsalicylate 1 cc intramuscularly twice a week

Dysentery

Dysentery or diarrhea as it is sometimes called is a symptom complex of frequent loose watery stools containing blood and mucus due to inflammation of the intestinal tract In general it may be divided into two distinct forms—the amebic and the bacillary

Amebic Dysentery

Amebic dysentery is an infectious disease either acute or chronic involving especially the large intestine though the small intestine and even the stomach may be included It is characterized by intermittent bouts of diarrhea and discharge of blood and mucus from the bowel Until recent years amebic dysentery was looked upon as a disease of the tropics but in reality it is a widespread infection throughout the world Its incidence is determined by the level of sanitation existing in the particular area It is estimated that about 10 per cent of people in the United States are infected with the disease

Etiology Amebic dysentery is caused by a protozoan or one celled organism known as *Entamoeba histolytica* the disease is contracted by the ingestion of the cyst of the ameba The organism undergoes three stages of development (1) The motile form is seen during the acute dysenteric period and when the warm fresh stools are examined under a microscope the amebae may be observed to be moving around (2) Then as the disease progresses a large number of amebae begin to form the cystic stage in which a genuine cyst with four nuclei develops in the intestines (3) It is this cyst excreted in the feces which is ingested by an individual and carried into the intestinal tract The cyst gives rise to eight motile amebae The trophozoites and cysts of this organism though excreted in the feces do not multiply outside the host The trophozoites degenerate rapidly and

may be found by the ninth or tenth day a negative reaction at the end of 30 days rules out Weil s disease

Differential Diagnosis During the early stage Weil s disease resembles any *acute infectious process The diseases which are most* apt to cause confusion are streptococcal infection of the throat influenza typhoid and paratyphoid fevers undulant fever acute catarrhal jaundice yellow fever and acute yellow atrophy of the liver Grippe *or influenza may simulate mild cases of Weil s disease however in* these two conditions the patient feels comparatively well when the temperature drops but he feels quite badly for several days after the temperature fall in Weil s disease The absence of rose *spots the* negative blood culture and cells in the spinal fluid usually eliminate the diagnosis of typhoid In acute catarrhal jaundice there is commonly a relatively low white blood count with a lymphadenopathy and a palpable spleen *while the opposite is true in Weil s disease* Renal disease hemorrhagic tendency and meningeal involvement are hardly ever present in catarrhal jaundice

Prognosis Mortality varies from about ten per cent in *endemic cases to 30 per cent in epidemics In general prognosis* is dependent on the age of the patient intensity of jaundice degree of renal failure heart function and severity of hemorrhagic diathesis Mortality increases with age and is highest in those over 60 years *An old axiom* states that where there is no jaundice there is no mortality An icterus index over 200 is a grave sign Renal failure or decreased heart function have an unfavorable effect on prognosis

TREATMENT

1 The general treatment is the same as that for any acute infectious disease

- *a* Patient should be kept in bed in a well ventilated room
- *b* *A light diet with plenty of fluid should be given If enough fluid* cannot be taken orally it should be administered subcutaneously or intravenously A 25 or 50 per cent glucose solution should be given if diuresis is desired while a five per cent solution is adequate to fulfill the fluid requirements
- *c* Headache and *myalgia may be relieved by aspirin and* codeine
- *d* Anemia may be combated with iron liver and vitamin B therapy Blood transfusions increase the red cell count rapidly and have a beneficial effect on the hemorrhages Vitamin K also has a good effect on bleeding

of blood and mucus and active amebic trophozoites If formed stools are passed only the cysts will be found Proctoscopic examination with smears taken of material from ulcerations are frequently of value

Prognosis Prognosis as far as the disease itself is concerned is quite satisfactory since death seldom occurs except in severe epidemics However while a patient does not usually die from the first attack repeated attacks which are not diagnosed or not properly treated may cause chronic invalidism and even death

One of the commonest and most serious complications is liver abscess though it is not seen so frequently now since the diagnosis is being made earlier and treatment has improved It may be found in carriers who have never actively had amebic dysentery or in patients who have long since recovered from the disease Frequently hepatic abscess is noted after hepatitis and if untreated ruptures into the lung pleura stomach and peritoneum There may be bowel perforation leading to peritonitis or abscesses of various parts of the body Obstruction may result from scar tissue forming in the intestine

TREATMENT

In general certain procedures must be carried out in the treatment of amebic dysentery The bowel and urine discharges should be disinfected with either five per cent cresol or chlorinated lime the linen bedclothes and other clothing should be soaked in cresol before washing

1 The patient should be put to bed and fed a light or liquid diet Boiled milk is especially recommended cocoa eggs custard or toast may be added It may be necessary to force fluids in small amounts or to administer them intravenously

2 In the presence of diarrhea intramuscular injections of emetine hydrochloride 0 066 Gm (1 grain) daily for 10 days are usually effective during the acute stage However this therapy does not cure the infection but only controls the alarming symptoms During the administration of this drug it is important to watch for toxic reactions as evidenced by a fall in blood pressure asthenia cardiac irregularity mental depression painful muscles and other signs This drug should be used with caution in the presence of heart disease The course of emetine should not be repeated without a 2 week

are destroyed by the digestive fluids but the cysts are much more resistant and carry the infection from man to man

The organism may enter the body through the gastrointestinal tract by way of contaminated drinking water, uncooked vegetables or contaminated food The food may be contaminated by excreta of patients convalescents or carriers of the disease

Pathology The *Entamoeba histolytica* penetrate the mucosa and submucosa of the large intestine causing discrete ulcers with slight inflammatory reaction No mucosal involvement is found between the ulcerations Secondly bacterial infection of the ulcers may occur causing an inflammatory reaction The amebae live and multiply in these lesions and cysts may be formed which pass into the feces and carry the infection to another host Amebic lesions may also affect other tissues and organs particularly the liver and occasionally the brain and lungs

Signs and Symptoms The incubation period varies from a few days to a few weeks The clinical picture is subject to extreme variation depending upon intensity of the infection and virulence of the strain Individuals may harbor the parasite for years and have only mild bouts of intermittent diarrhea and be completely symptom free during remissions They complain only of undue fatigue and malaise with vague gastrointestinal complaints

The more acute form is characterized by intense diarrhea with cramping lower abdominal pain and tenderness over both lower quadrants and colon The stools are small numerous and may contain blood and mucus

Acute amebic dysentery is relatively uncommon and has an abrupt onset in about half the cases This is particularly true when the disease is complicated by bacillary dysentery In some cases the dysentery may remain latent or quiescent for a long period of time and the patient believes he is cured although there is a residual focus of infection in the large intestine This may be aggravated by infection trauma and alcohol

Diagnosis The acute form of amebic dysentery is very much like the bacillary type however in the latter the patient is usually somewhat toxic and may show fever and leukocytosis, though these features do not rule out the amebic form A definite diagnosis can be made from a study of the warm fresh stools containing quite a large amount

sone by mouth combined with retention enemas of chiniofon has been successful in many cases

7 Amebic hepatitis should be treated with a course of emetine prior to any possible surgical intervention

Prophylaxis The cysts or encysted form of *Entamoeba histolytica* are not destroyed by chlorination or hyperchlorination of water Consequently water from questionable sources should be adequately filtered or distilled prior to use

Bacillary Dysentery

Bacillary dysentery is an acute infectious disease due to toxins generated by the Shigella dysenteriae and characterized by diarrhea abdominal pain tenesmus mucus and blood in the stools and toxemia

Etiology The disease is especially prevalent in tropical countries but it may occur in any part of the world It is most apt to occur where sanitary conditions are poor or overtaxed as in prisons military camps and other situations The etiological agent is the dysentery bacillus of the genus Shigella The classification of the Shigella on page 460 is given in *Notes on Tropical and Exotic Diseases of Naval Importance* published by the United States Naval Medical School

Human beings become infected by the ingestion of food and drink which has been contaminated by patients with bacillary dysentery or carriers of the disease Flies also help to spread the infection

Pathology The intestines are particularly affected and there is diffuse catarrhal inflammation of the colon often extending above the ileocecal valve As the disease progresses the inflammation may increase to necrosis and ulceration of the mucosa associated with a superficial exudate There is thickening and edema of the wall of the colon The most severe reactions are found in the rectum Severe cases present necrotic ulcerated mucosa covered with a greenish purple membrane while milder cases may show only discrete superficial ulcers separated by inflamed mucosa Under the layer of necrosis are small sharply circumscribed or diffuse hemorrhages with small red spots scattered about them Ulcers may persist after the acute infection and form a focus for chronic infection This may be the reason some carry the disease for long periods of time

period of rest after initial treatment Bismuth subnitrate in large doses 2 Gm (30 grains) four times a day may be given in addition to emetine

3 Emetine bismuth iodine, in 0 133 Gm (2 grains) capsules may be given about four hours after the evening meal for ten nights If given in tablet form with stearin there is a tendency for it to be *passed unabsorbed in the feces thus* proper absorption is an important factor in the administration of the drug Luminal 0 66 Gm (1 grain), effectively combats nausea and vomiting in most cases though allonal or 0 66 cc (10 minims) of tincture of opium may be more satisfactory Emetine periodide is less toxic than the above preparation but is not as effective

4 In the chronic or cystic stage of dysentery diarrhea is not a prominent symptom or it may be absent and in these cases emetine is of little value since it has practically no effect on the cysts or lumen dwellers Sir Philip Manson Bahr introduced a combination of quinoxyl retention enemata by day and emetine bismuth iodide by mouth at night Usually a 2 per cent sodium bicarbonate enema is given first followed by a quinoxyl retention enema 200 cc of 2½ *per cent solution These may* be retained for four to eight hours and are well tolerated even a five per cent solution is without disagreeable effects in refractory cases This therapy combined with emetine bismuth iodide is continued for 10 to 12 days the *patient is given as* much breakfast and dinner as he wishes but no supper Chiniofon as this drug is sometimes called may also be given by mouth in four 0 266 Gm (4 grains) doses after each meal for a week If the stools remain positive therapy should be discontinued for a week and then a new course started If two courses fail diodoquin in 1 66 Gm (25 grains) daily doses for two or three weeks should be tried

5 Vioform 0 266 Gm (4 grains) in capsules three times a day for ten days *has been recommended instead of chiniofon* It is a chlorine derivative of quinoline and has a much higher percentage of iodine Both this substance and chiniofon act on cysts and motile forms

6 Carbarsone 0 266 Gm (4 grains) twice daily for ten days has been suggested However because it is an arsenic compound there is danger of poisoning which may outweigh its effectiveness It must not be given to patients with kidney or liver damage Carbar

In the bowel contents the inflamed areas and sometimes the mesenteric glands there are many bacilli Bacilli are not usually found in the blood stream or urine

Signs and Symptoms Symptoms may vary from those of mild diarrhea without fever to those of great intensity Typically the onset of dysentery is sudden and accompanied by fever abdominal cramps and the passage of loose watery greenish or yellow stools Later the stools become bloody and mucopurulent Tenesmus vomiting prostration, toxemia and dehydration are prominent in severe cases The disease may be followed by neuritis or arthritis and sometimes also by conjunctivitis iritis otitis or myocarditis

Diagnosis This is made by the identification of species of Shigellae from stool cultures and this is done most easily in the early part of the disease Several cultures may be required and stools should be examined as soon as possible after being passed Selective culture media as desoxycholate citrate agar S S are best Agglutination reactions with the patient s sera and known antigens have been done but are not so practical especially in the early stages Microscopic examination of the stools on an unstained slide will show an absence or marked reduction of fecal elements red cells often in rouleaux many pus cells desquamated epithelium numerous macrophage cells and ghost cells

In the absence of laboratory facilities particularly when the case is complicated by toxemia or in the presence of epidemics diagnosis may be made with reasonable assurance when on gross examination the stools appear mucosanguinous with a purulent exudate mixed with the feces

Prognosis Prognosis depends on the severity of an attack and on the age and condition of the patient Infants and older individuals have a higher mortality The presence of complications is unfavorable prognostically and severe intestinal symptoms with collapse offer a poor outlook

TREATMENT

1 Absolute bed rest is necessary

2 The diet should be liquid or soft with low residue until the stools are formed In very severe cases it should be supplemented with vitamins

Name of Organism	*Common Terms of Designation*	*General Properties in Relation to Dysentery*
Shigella dysenteriae	Shiga's bacillus	Only organism in group producing a true soluble exotoxin Causes severe form of dysentery Commonly found in Orient
Shigella flexneri	Numerous types Occasionally divided into various cultural types Flexner Hiss Y and Strong bacilli More correct to divide into serologic types depending on composition of antigens V W X Y and Z	World wide distribution Frequently causes severe dysentery may produce mild illness Common cause of outbreaks in jails asylums military camps etc
Shigella sonnei	Sonne bacillus	Frequent cause of dysentery World wide distribution High degree of contagiousness Frequently causes a mild disease often not recognized clinically which may account for much of its spread May cause severe dysentery
Shigella ambiguus	Schmitz's bacillus Culturally similar to S dysenteriae	Infrequent cause of dysentery generally produces a relatively mild illness
Shigella newcastle	Newcastle bacillus	Recently discovered organism has been observed with increasing frequency Wide distribution
Shigella alkalescens	Bact alkalescens	Does not cause true dysentery Reported as cause of food poisoning
Shigella dispar	Dispar bacillus Culturally similar to S sonnei May be mistaken for it	No evidence that it causes dysentery May be regarded as non pathogenic

Etiology The *Vibrio cholerae* is responsible for this malady and the infection is carried chiefly by man through carriers and patients Humid warm climates favor the incidence of the disease The *V cholerae* is transmitted by contaminated food and water due to faulty personal hygiene and public sanitation or the handling of food by carriers Flies roaches and other insects may aid in the spread of infections Dangerous foods include melons lettuce salad greens berries celery milk fish and water If these foods are taken in the Far East extreme care should be taken to see that they have not be come infected

Pathology The lower portion of the intestines are most affected by the cholera endotoxin Rigor mortis emaciation a leaden skin color and shriveled hands are characteristic of the cadaver

Dehydration is prominent in the internal structures The muscles appear dark red and dry the lungs are usually small and shrunken The most important changes are in the abdomen The omentum is dry and shriveled The intestines are a pinkish purplish color and have a ground glass appearance The affected intestinal mucosa is congested and the lumen contains an alkaline fluid which presents the appearance of rice water The bowel may contain foul smelling brownish material if the death is late in the course of the disease Parenchymatous nephritis is the rule Acute cholecystitis is common If death is early venous congestion is less marked and the stools are more moist

The severe surging diarrhea results in marked fluid loss and con sequent electrolyte imbalance This is reflected by the marked drop in the carbon dioxide combining power of the blood and the increase in the specific gravity of the blood from a normal of from 1 056 to 1 058 to about 1 070 Hemoconcentration is further indicated by the high value for the red cell count hemoglobin percentage and cell pack *volume*

Signs and Symptoms The vibrios undergo lysis in the small bowel and release a powerful toxin The incubation period is from one to five days and is followed by severe purging diarrhea associ ated with excessive vomiting dehydration anuria muscle cramps and collapse The rectal temperature is from 39 *to 40° C* (102 to 104 F) In spite of the prostration the patient is conscious Peripheral circulation is diminished the patient is in intense collapse and presents a leaden shrunken facies The blood is thick dark

3 Enough fluid to insure a urinary output of 1200 to 1500 cc daily, usually about 3000 cc must be provided In severe cases intravenous fluid is needed and physiological salt solution with five per cent glucose in amounts large enough to insure a 1200 to 1500 cc output of urine daily should be given Intravenous plasma 500 to 1000 cc should be administered to combat shock but not until the dehydration is controlled

4 Codeine or morphine may be used for the relief of pain Belladonna and chloral hydrate in combination with codeine may also do good or paregoric, 1 to 2 cc (15 to 30 minims) may be given after each stool until 20 cc (⅔ ounce) have been taken in 24 hours

5 Sulfadiazine is the sulfonamide of choice in an amount of 4 to 6 Gm (60 to 90 grains) a day For the acute case the initial dose is 2 Gm (30 grains) followed every 4 hours day and night by 1 Gm (15 grains) Chemotherapy is to be used in acute diarrheas and diseases with dehydration only when appropriate measures have been taken to restore and maintain the normal hydration If there is no therapeutic response within 4 to 5 days poorly absorbed sulfonamides such as sulfaguanidine or sulfasuxidine may be used in an amount of 20 Gm (300 grains) a day in divided doses

6 Monovalent antiserum for S dysenteriae may be used but not until after bacteriological confirmation of the diagnosis The dosage is 40 to 80 cc intramuscularly or intravenously every day until the toxemia and dysentery become improved Intramuscular doses are best given into the buttocks Intravenous doses should be diluted in 500 cc of normal saline and given slowly Sensitivity tests before therapy are indicated Polyvalent antidysentery serum is of doubtful value

7 Measures such as purgation high enemas and colonic irrigations and bacteriophage are not recommended

Cholera

Cholera is an acute infectious disease caused by the bacterium *Vibrio cholerae* Excessive diarrhea vomiting cramps in the muscles anuria and collapse mark the course of the disease The disorder has been known since ancient times and occurs in epidemics and pandemics It was introduced to the eastern United States in 1832 and to the western states in 1850 At present it is still common in Asia and the Far East

2 The diet should be low in residue and supplemented by vitamin B complex and ascorbic acid 100 mg daily Nausea and vomiting may prevent the intake of food

3 Excellent results have been reported with a condensation product of sulfathiazole and formaldehyde known as Compound 6257 An initial dose of 6 Gm (90 grains) is given followed 4 hours later by 4 Gm (60 grains) and 2 doses of 4 Gm (60 grains) on the second day and 1 Gm (15 grains) morning and evening for the next 5 days The drug has been of some value prophylactically

4 Unless nausea prevents the patient should be given as much fluid as he can take Water lactate Ringer s (Hartman s) solution 5 per cent dextrose and 0 75 per cent lactic acid in normal saline (1 tablespoon sugar and 20 drops of lactic acid per 100 cc —3 ounces—saline) or a bouillon cube containing 2 4 Gm salt dissolved in a cup of hot water and cooled are all satisfactory for oral use

Normal saline Ringer s solution five per cent dextrose in normal saline and lactate Ringer s (Hartman s) solution are recommended for parenteral use The amount needed may be judged by the patient s blood pressure thirst and appearance Moderately severe cases require 2000 cc in the first hour In extreme cases this should be repeated every two or three hours Blood or plasma transfusions should follow fluid therapy three to six hours after dehydration has been relieved

If water intoxication occurs the excess fluid can generally be removed by giving a salt free diet reduced fluid intake sweating catharsis and plasma In the case of prolonged fluid therapy 10 to 30 mg (⅙ to ½ grain) thiamin hydrochloride should be given daily by mouth or parenterally To prevent tetany 5 to 10 cc of sterile ten per cent calcium gluconate may be necessary intramuscularly or intravenously If acidosis is present 1000 to 2000 or more cc of lactate Ringer s (Hartman s) solution should be administered intravenously or subcutaneously and repeated in six or eight hours if necessary If lactate Ringer s solution is unobtainable sodium bicarbonate may be used but it may cause alkalosis and tetany Sodium bicarbonate solution may be made by dissolving 5 75 Gm (86¼ grains) sodium chloride in 1000 cc distilled water and sterilizing by boiling This solution is removed from the heat and 18 15 Gm (272¼ grains) of sodium bicarbonate which has been weighed and

and tarry The leukocyte count is from 12 000 to 50 000 Blood pressure is low

This collapse stage may be followed by rising temperature with clinical improvement or by anuria and a uremic death The disease may be complicated by anuria uremia cholecystitis jaundice and miscarriage in pregnant women

Diagnosis Bacteriological diagnosis can be made by examining *stained slides of flecks of mucus from the stools* This material *may be enriched in alkaline* peptone solution for four to *eight hours* Following this it should be cultivated on Dieudonné s media Agglutination tests with known antisera and suspected organisms should be done The typical cholera red reaction may be elicited by adding six to eight drops of concentrated sulphuric acid to a culture grown in Dunham s peptone medium for 24 to 48 hours Pfeiffer s phenomena is another diagnostic aid though a positive result does not always indicate cholera This is a bacteriolytic reaction A loopful of the suspicious organisms should be suspended from an agar slant in a milliliter of saline or peptone solution and mixed with a milliliter of cholera antiserum This material is injected into the peritoneal cavity of a guinea pig In 20 40 and 60 minutes a drop or so of the peritoneal fluid should be removed with a glass capillary pipette and *examined microscopically If V cholerae are* present they will lose their motility and disintegrate A control with no antiserum or with normal serum should be used

Diagnosis is based on clinical findings and laboratory data It should be confirmed if the patient dies by a postmortem examination The differential diagnosis includes *food poisoning* mushroom poisoning malaria and bacillary dysentery Laboratory tests are valuable in excluding these entities

Prognosis Prognosis is serious since about 50 per cent of these patients die Early treatment affects prognosis favorably Cholera is especially lethal in the young and aged and the outcome *is doubtful* in those with kidney disease those who are addicted to alcoholism or pregnant women

TREATMENT

1 The *patient must be kept in bed* and *heat* should be applied to the abdomen and arms and legs as needed

2 The diet should be low in residue and supplemented by vitamin B complex and ascorbic acid 100 mg daily Nausea and vomiting may prevent the intake of food

3 Excellent results have been reported with a condensation product of sulfathiazole and formaldehyde known as Compound 6257 An initial dose of 6 Gm (90 grains) is given followed 4 hours later by 4 Gm (60 grains) and 2 doses of 4 Gm (60 grains) on the second day and 1 Gm (15 grains) morning and evening for the next 5 days The drug has been of some value prophylactically

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placed in a sterile container is added immediately This is cooled to body temperature and used at once The three ingredients used should never be mixed together at the same time and sterilized by boiling or autoclaving as this converts the bicarbonate to caustic *carbonate Great care should be used in the administration of this* preparation in order to prevent complications

Prophylaxis Vaccination affords a great deal of protection against cholera Booster injections are required annually or more often in the presence of the disease

Ascariasis

Ascariasis or roundworm infection is an infection of the small intestine caused by the *Ascaris lumbricoides* the most common helminthic parasite of man

Etiology *Ascaris lumbricoides,* the largest intestinal nematode infection usually occurs by swallowing ova It may be conveyed to the mouth by dirty fingers or by contaminated water green vegetables or other foods The ova hatch in the small intestine and burrow into the gut and pass into the blood stream and are carried to the heart and lungs They break through the pulmonary capillaries into the air sacs and pass by way of the bronchi trachea and esophagus back to the small intestines where they mature

Pathology Small hemorrhages may occur at the penetration site of the parasite through the intestinal wall or into the lung alveoli *Pneumonitis* may be caused by *the passage of the parasites* through the lung The presence of a large number of adult parasites may form a bolus causing intestinal obstruction The parasite infrequently causes appendicitis

Signs and Symptoms Intestinal colic is the chief complaint and may be associated with anorexia and insomnia The worms may gather in clumps to produce intestinal obstruction They may also migrate up or down the intestinal tract and into the *appendix* bile ducts gallbladder pancreatic ducts nose sinuses middle ear and larynx where they can cause unusual and serious disturbances The worms may sometimes be vomited or they may escape from the nostrils Intestinal ulcers and infections occasionally develop Eosinophilia occurs

Diagnosis Diagnosis is made by the discovery of the character

istic eggs in the feces or by the spontaneous passing of adult worms

Prognosis Prognosis is good as a rule though at times the abdominal symptoms may require operation If the pulmonary system is involved careful nursing is necessary for recovery

TREATMENT

Hexylresorcinol crystoids (caprokol capsules) are given to expel the worms as indicated in the treatment of hookworm Two hours later a saline purge is administered to remove dead and dying worms Other drugs as santonin 0 1 to 0 2 Gm (1½ to 3 grains) for adults and 0 01 Gm (3/20 grain) for each year of age for children followed by a saline purge or oil of chenopodium have been used but they are apt to be very toxic If the larvae are migrating through the body they cannot be killed

LOUSE- AND TICK-BORNE GROUP

Prophylaxis Infection with body lice can be avoided by cleanliness and by wearing clothing impregnated with a lousicide such as DDT The attendants caring for patients should in addition wear protective masks goggles and gloves while caring for the patients and maintain strict isolation technique When a patient is suspected of having a louse borne disease he should be deloused and put in a louse free room His former surroundings should be deloused and quarantined All blankets and clothing should be disinfected The patient s head should be clipped and dusted with DDT and the skin bathed followed by an application of a light oil

Tick infested areas should be avoided when possible Protective clothing impregnated with dimethyl phthalate should be worn when in an endemic area In addition careful inspection of the body surface should be made at 3 hour intervals to remove such ticks as may have entered the clothing or become attached to exposed skin If ticks can be removed before they have been on the body long the disease may be prevented since ticks must remain attached for some time before they can transmit infection Ticks should be removed with forceps or a piece of paper rather than with the bare fingers Hands should be carefully washed with soap and water after removing ticks

Plague

Plague is an acute febrile disease attended by a very high mortality rate Black death Oriental plague and pest are other names given to this malady The disease has been known since ancient times and has occurred frequently in devastating epidemics It begins with chills and fever followed in a short time by great prostration swelling of the lymphatic glands the formation of buboes in the femoral, inguinal and cervical regions primary or secondary pneumonia septicemia and petechial and diffuse hemorrhages Delirium headache, vomiting and diarrhea are associated symptoms

Etiology The pathogenic organism is *Pasteurella pestis* The disease is usually transmitted to man by fleas which have fed on infected rats or wild rodents The pneumonic type of plague may be passed by droplet infection or by human expectoration feces urine and the discharge from buboes

The disease may be of two kinds classical plague a disease of domestic rats which may be transmitted to man and sylvatic plague a disease of wild rodents transmissible to man Classical plague is found chiefly in Asia but also occurs in Africa and South America Sporadic cases occur in ports in any part of the world Sylvatic plague occurs chiefly in South America Argentina and the Transbaikal regions of Siberia It has been found in western United States and Canada

Pathology The infection is usually acquired through cutaneous inoculation but the site of entrance is seldom apparent The pathological changes are characterized by marked congestion and hemorrhagic edema of the lymph glands The primary bubo is surrounded by hemorrhagic extravasations of connective tissue and there is periglandular edema The toxin of the plague bacillus has an extremely destructive effect on the endothelial cells of the blood vessels and lymphatics resulting in extravasations of blood typified by petechial spots of the skin and serous membranes The organs of the body are congested including the brain but meningitis is not a feature The heart is dilated and the spleen may also be enlarged

Signs and Symptoms There are three clinical types of plague—bubonic septicemic and pneumonic The bubonic type is common

est especially in warm climates and comes on suddenly with severe headache high fever and leukocytosis The lymph nodes enlarge and become painful and indurated Buboes occur most frequently in the inguinal region then the axillary and cervical areas Conjunctivitis is prominent Prostration is intense and the patient may be delirious excited and anxious Mucosal and subcutaneous hemorrhages are present and petechiae and ecchymoses are evident The average incubation period is from two to seven days If the patient remains alive for five days his chances of survival are good Some mild cases may remain ambulatory and in such instances the first symptom may be a painful bubo

Septicemic plague is primary or secondary In bubonic or pneumonic plague there may be secondary septicemia Primary septicemic plague starts in the mucous membranes of the eyes mouth or throat and is usually followed by death Symptoms resemble bubonic plague except the localized buboes are not found The temperature may be low due to the overwhelming infection The incubation period for this form of plague is two days and death may ensue in another two days

Pneumonic plague may also be primary or secondary The secondary form occurs in a small percentage of the cases of bubonic plague and these secondary cases may cause primary pneumonic epidemics especially in colder climates and where living conditions are crowded Primary pneumonic plague is contracted by droplet infection of the respiratory mucosa or conjunctivae or directly from infected rats It is characterized by a sudden onset fulminating course fever and mucoid bloody sputum Death occurs as a rule

Diagnosis A smear of aspirated contents of buboes or sputum stained with methylene blue shows the bacilli as short organisms with bipolar staining and swollen vacuolated involution forms A culture taken from a bubo blood or sputum on nutrient agar or in broth shows characteristic gram negative organisms Mice rats and guinea pigs when inoculated intraperitoneally or by skin will die in two or three days and autopsy will show organisms and changes typical of plague Care must be taken to see that the animals are free of fleas or other insects Aseptic technic is important In all laboratory tests great care must be taken in handling infected material

Prognosis Plague is the most serious of epidemic diseases In principally the pneumonic and septicemic varieties the outlook is almost invariably fatal In bubonic plague mortality ranges from 60 to 90 per cent Under adequate therapy there has been a very marked improvement

TREATMENT

1 Morphine and sponging may relieve the restlessness and fever Fluids should be forced both orally and parenterally

2 Sulfathiazole or sulfadiazine sometimes brings about good results The initial dose is 4 Gm (60 grains) followed by 1 5 Gm (22½ grains) every four hours day and night until the temperature has been normal for seven days In serious cases sodium sulfathiazole may be given intravenously in five per cent solution of water 0 06 Gm (9/10 grain) per kilogram (2 2 pounds) of body weight This is to be followed every six hours by 0 03 Gm (5/10 grain) per kilogram (2 2 pounds) of body weight Oral sulfonamide therapy should be resumed as soon as possible

3 Good results have been reported with streptomycin 1 Gm (15 grains) a day given in 3 hour intervals in divided doses for 72 to 96 hours

4 The use of hot wet applications on the buboes may aid in localizing the infection Incision is not recommended until localization is complete as blood stream infection may occur

Prophylaxis Strict isolation of infected individuals and the sanitary disposal of all discharges is important in addition to the usual precautions protecting attendants against bites by fleas or contamination with infected material

Buildings should be rat proofed and rats should be exterminated Dead or dying rats should be examined for plague as a rat dead of plague may be the first warning of the onset of a human epidemic In rural areas wild rodents should be avoided and care taken that they do not come near the food supply Ships should be examined for rats periodically and if rats are found they should be killed

Vaccination is a valuable preventive measure and gives protection for two years Vaccine made from two billion dead *Pasteurella pestis* per 1 ml is used The first injection is 0 5 ml and a second injection following in a week to ten days is 1 0 ml Injections of 1 ml are then given when indicated to boost immunity

Typhus Fever

Typhus fever is an acute specific contagious disease caused by rickettsia and conveyed from man to man by the human body louse in the epidemic type and from rat to man by rat fleas in the murine type It is characterized by an abrupt onset a high continuous fever purpuric eruptions and central nervous system symptoms The disease terminates by crisis or rapid lysis from the tenth to the fourteenth day Brill s disease is the name applied to mild sporadic cases of epidemic typhus not associated with louse infestation occurring in foreign born Americans

Etiology Typhus fever is caused by the *Rickettsia prowazeki* which are tiny rod shaped gram negative organisms The disease is commonest among poor people who live in overcrowded and dirty areas and is infectious by contact with the patient or with bedding or clothing *It is commonly seen in epidemic proportions in mass displacements of people associated with wars and floods* However ordinarily the organisms are deposited on the skin by the flea or louse and enter the blood stream when the skin is scratched or punctured Typhus fever is known to be one of the great epidemic diseases of the world Outbreaks have occurred during almost every war in Europe but it is comparatively rare for one to occur in peacetime under modern sanitary conditions The epidemics occur most frequently in the winter an explanation for this fact is that fewer baths are taken and clothing is changed less often thus creating an agreeable situation for louse propagation

Pathology Typhus fever pathology is nonspecific consisting of endothelial proliferation of the arterioles and capillaries leading to thrombosis hemorrhagic manifestations and gangrene There is accompanying perivascular round cell infiltration These changes are found chiefly in the skin central nervous system and myocardium Cloudy swelling of the myocardium spleen liver and kidney are frequently observed

Signs and Symptoms The incubation period is from 10 to 12 days and at the end of this time there may be slight fever headache and general malaise On the other hand this early stage may be lacking and instead the disease sets in abruptly with chills rigors fever rising to 40 C (104 F) with proportionate pulse nausea and vomiting and body pains Intense headache is usually the outstanding

symptom The conjunctivae are injected pupils contracted face tense hot and flushed and the tongue is thickly furred Patients are usually excited and may be stuporous Delirium is common

About five days after onset the typical rash appears first on the abdomen upper chest and hands and spreading to the trunk and extremities but seldom to the face The lesions are rose-colored macules which disappear on pressure They may be overlooked in the beginning because of erythema in some cases Moderate leukocytosis is commonly noted and if marked is a serious sign Cough and rales in the chest are common findings The rash becomes more pronounced depending on the severity of the disease and the lesions increase in size and progress in color from rose red to deep purple If the temperature falls while the patient is in a state of coma prognosis is guarded If a distinct improvement is noted in the clinical picture about the twelfth day and the delirious patient becomes quiet recovery is probable Fever usually declines by lysis

Bronchitis and pneumonia are the most frequent complications the latter causing most fatalities Occasionally death is due to myocardial degeneration Gangrene of the extremities bed sores neuralgia and neuritis may also complicate the picture Thrombosis of the large arteries as well as of the small cutaneous vessels resulting in gangrene of the skin is frequently noted

Diagnosis Until the rash appears the clinical picture of typhus resembles that of any acute infectious disease and offers difficulty in diagnosis unless an epidemic prevails Blood examination for parasites will rule out malaria and relapsing fever Typhoid fever can usually be differentiated because the mode of onset symptoms and severity of rash are different The possibility of a diagnosis of pneumonia must be considered Measles smallpox and scarlet fever are distinguishable by their rash Rocky Mountain spotted fever may offer some difficulty in diagnosis from endemic typhus The Weil Felix reaction is positive in typhus fever after the fifth day and the titer increases for a few days before tapering off and may continue to be positive for weeks or months The complement fixation test becomes positive after the disease has been present for a few weeks Rickettsial agglutination is another valuable diagnostic procedure becoming positive at the end of the first week

Prognosis The mortality rate for the epidemic louse borne typhus ranges from about 10 to 70 per cent while the endemic rate is as low as five per cent Few young people die of the disease but the mortality is higher amongst the older individuals since pneumonia is more likely to develop and the disease as a whole is much more severe Murine typhus is generally a milder disease than the louse borne epidemic type

TREATMENT

1 When a patient is suspected of having typhus he should be deloused and put in a louse free room his former surroundings should be deloused and quarantined All blankets and clothing should be disinfected The patient s hair should be clipped the skin bathed and a light oil such as kerosene which is an old standby should be applied

2 Treatment is symptomatic rather than specific and is directed at supporting the patient General therapeutic principles should be employed Continuous bed rest in a quiet well ventilated room with experienced nursing care is important The position of the patient should be changed from time to time to prevent hypostatic congestion and bed sores

3 A semisolid or liquid diet with plenty of fluid orally interstitially or intravenously should be given If the patient is delirious or comatose foods should be given by tube

4 Fever may be lowered by tepid sponge baths and ice bags applied to the head

5 Stimulants as coramine 1 to 3 cc of a 25 per cent solution or caffeine sodium benzoate 0 33 to 0 5 Gm (5 to 7½ grains) subcutaneously or intramuscularly may be given

6 Every effort should be made to conserve the strength of the patient Cough mixtures containing sedatives should be given for the relief of exhausting cough Chloral hydrate 1 to 2 Gm (15 to 30 grains) should be given orally or rectally to overcome the insomnia and hyoscine 0 0005 Gm (1/100 grain) hypodermically with or without morphine may be used if the patient is violently delirious

7 Oral hygiene is important and the mouth should be washed out at frequent intervals daily using either normal saline sodium perborate or hydrogen peroxide

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may be infiltrated and prominent Smears made from the liver and spleen reveal spirochetes

Signs and Symptoms The onset of the louse borne variety is sudden with chills persistent high fever of 40 to 40 5° C (104 to 105 F) for four to six days headache vomiting enlargement of the spleen albuminuria and leukocytosis The fever drops by crisis There may be an asymptomatic afebrile period of four to eight days followed by a relapse but during relapses symptoms are not as severe as the first attack Relapses may occur more than once but immunity seems to increase with each relapse Jaundice delirium vertigo and hemorrhages may occur The tick borne type presents similar symptoms except that the cerebrospinal symptoms are commoner in some areas and there are more relapses usually at least four The paroxysms are more intense but of shorter duration

Complications are serious and include pneumonia intense jaundice diarrhea herpes iritis hemorrhages from the nose stomach and kidneys In the cases with jaundice myocarditis may occur There may be a meningismus resembling that of cerebrospinal meningitis

Diagnosis The Borrelia may be demonstrated in the blood during the febrile period by dark field examination by Giemsa stained thin or thick films or by mouse inoculation which becomes positive within three days

Relapsing fever must be differentiated from dengue malaria cerebrospinal meningitis plague typhoid trench fever, and typhus The absence of leukopenia postorbital pain and presence of a tender spleen will exclude dengue Identification of parasites will differentiate malaria but the two diseases may coexist

Prognosis Prognosis is usually 2 to 5 per cent in uncomplicated cases In some African epidemics a mortality of 50 per cent has been reported

TREATMENT

1 Mapharsen 0 06 Gm (60 mg) or neosalvarsan 0 3 to 0 9 Gm (5 to 15 grains) is indicated as soon as the diagnosis is made A single injection given early when the temperature is rising may be adequate However these drugs should not be used in the afebrile period or near a crisis If the patient does not respond to neosalvarsan bismuth

8 Para amino benzoic acid may be given as follows

The initial dose of 0 05 Gm (5/6 grain) per pound or 8 Gm for a 160 pound man with a maintenance dose ranging from 1 to 3 Gm given at 2 hour intervals The drug should be continued for at least 48 hours after the temperature has been normal When this drug is being administered certain precautions should be followed

a Urine maintained neutral or alkaline to prevent precipitation in the tubules by the use of alkalies

b Daily blood counts and differentials discontinuing the drug as the white count drops below 3000 per cu mm or the polymorphonuclear cells below 25 per cent

c Secondary bacterial infection should be treated with penicillin since sulfonamides appear to exert a deleterious effect in rickettsial in fection

9 Chloromycetin has been reported of value in a small series of cases

Prophylaxis The following must be remembered in prophylaxis A high degree of protection is afforded by typhus vaccine 1 cc is given subcutaneously at weekly intervals for three doses with stimu lating doses every 6 months

Relapsing Fever

Relapsing fever is an infectious disease caused by a spirochete transmitted to man by lice or ticks

Etiology Two types of organisms are involved *Borrelia recur rentis*, which is passed to man by the louse and *Borrelia duttoni* which is carried by ticks Louse borne relapsing fever has occurred in all the continents of the world with the possible exception of Aus tralia It is common in Eastern Europe where many severe epi demics have occurred as well as in Africa India Asia and in the Americas

Tick borne relapsing fever does not occur in epidemics but out breaks are localized to the place where the ticks are found The malady occurs in Africa Asia Europe Central America and South America

Pathology Visceral hemorrhages nose bleed jaundice and bile stained viscera are characteristic The spleen is soft and enlarged and may present infarctions On cut surface the malphigian bodies

in the liver and focal brain changes have also been reported by some

Signs and Symptoms The incubation period is from 3 to 14 days The symptoms resemble those of endemic typhus and their severity varies Usually there is a frontooccipital headache pain in the back and severe malaise Muscle and bone pain sweating sensitive inflamed eyes nausea and vomiting are characteristic Later there may be delirium asphasia ankle clonus incoordination cyanosis apprehension Kernig s sign and opisthotonos In two to five days a rash appears first on the wrists and ankles and spreading to the legs upper back outer surface of the arms buttocks palms soles scalp forehead the inside of the mouth and pharynx The rash is rose colored and the result of vascular inflammation In some cases extensive necrosis of the buttocks external genitals and dependent parts of the body occurs By the end of the third week the fever drops rapidly by lysis

During the course of the disease there is frequently hepatomegaly and splenomegaly and jaundice may become evident The white cell count is commonly elevated as are the mononuclear cells The number of lymphocytes is decreased and moderate anemia is present The spinal fluid is normal

Rocky Mountain spotted fever may be complicated by pneumonia phlebitis hemorrhages hemiplegia iritis nephritis Convalescence is slow

Diagnosis Diagnosis is based on the history of exposure to ticks fever headache rash and central nervous system symptoms The complement fixation test becomes positive at the end of the second week and is valuable in differentiating this disease from others caused by rickettsia In these serological tests it is the rise in the titer of the second and subsequent blood samples that is of significance The disease may resemble several types of typhus making differentiation difficult Measles typhoid and cerebrospinal meningitis must be excluded Measles may be ruled out by the absence of Koplik spots and initial coryza typhoid and meningitis by laboratory tests

Prognosis The overall prognosis of Rock Mountain spotted fever in the United States is 22 per cent The prognosis is more serious in older than younger persons and is worse in those with increased nervous symptoms

preparations as sodium potassium bismuth tartrate 0 02 Gm (0 3 grain) in 2 ml of distilled water may be given intramuscularly

2 Good nursing care and symptomatic treatment are necessary The patient may become very hungry during or after a crisis but overfeeding may cause diarrhea

3 Convalescent serum may be of benefit

4 The heart and circulation should be watched During crises there may be collapse with shock

Rocky Mountain Spotted Fever

Rocky Mountain spotted fever is a rickettsial disease transmitted by ticks and characterized by chills moderate fever severe pains in muscles and joints rash headache and delirium

Etiology The disease is caused by *Rickettsia rickettsi* and is transmitted only by ticks The reservoir hosts are probably small field rodents in the West and dogs in the East In the East the dog ticks *Dermacentor variabilis* are responsible for this malady and in the West the *Dermacentor andersoni* Other types of ticks may be vectors in other places Rocky Mountain spotted fever is commonest in spring and early summer in the northwestern states in the East and South through the summer This disorder occurs in all states of the Union except Maine Vermont New Hampshire Connecticut Rhode Island Michigan and Wisconsin it is also found in Canada Brazil and Colombia

Pathology At postmortem the body may be jaundiced The blood is dark fluid slow to clot and venous engorgement is prominent Petechial spots may be apparent on the extremities and trunk Splenomegaly and enlargement of the lymph glands have been noted Pathology resembles that of typhus fever The outstanding feature in the histopathology is the distribution and character of the blood vessel lesions in the skin and subcutaneous tissues muscles and in the testes and their appendages There are almost always hemorrhages into these tissues Vascular lesions occur in the vessels of almost all parts of the body and consist of proliferative reactions of the endothelium at first These reactions are followed by necrosis with thrombus formation Rickettsiae are found in the endothelium and smooth muscle cells of the blood vessel walls Focal necrosis may be present

heart trouble frequently develop Changes in rhythm and disturbances of conduction dyspnea and precordial pain are common evidences of cardiac involvement occurring in the chronic stage of the disease

Diagnosis Diagnosis is confirmed on demonstration of the trypanosomes in the blood This is not usually possible except in the acute febrile stage Guinea pig or puppy inoculation with 10 cc of blood from the patient is often helpful The animal inoculated will have trypanosomes in the blood in about two weeks Complement fixation tests are useful if a reliable antigen is present

Prognosis Prognosis is worst in the first year of life The mortality rate is five per cent or more

TREATMENT

Treatment is symptomatic Measures should be taken to prevent the bites of the Triatoma and other vectors It is often difficult to control patients as many in fact most of them are poor and illiterate Their dwellings often favor the survival of the vectors and should be avoided Mosquito nets over beds are good Animal hosts should be controlled

TREATMENT

The treatment of Rocky Mountain spotted fever is as follows

1 Para amino benzoic acid in similar dosage to that given in typhus fever may be administered

2 Chloromycetin and aureomycin have been reported of marked value in this disease

3 Acidosis is combatted by the use of alkalies orally or sixth molar sodium lactate intravenously or subcutaneously

4 Lowered serum protein caused by vascular damage starvation or liver failure is treated with plasma serum albumin

5 Multivitamins with particular emphasis on thiamine ascorbic acid B complex and K are indicated

6 Hyperimmune serum is of value early before or shortly after the appearance of a rash

7 Vaccination is beneficial in prophylaxis

American Trypanosomiasis

American trypanosomiasis is a specific parasitic infection characterized by severe lymphadenopathy anemia and localized edema affecting chiefly children

Etiology This disease is caused by *Trypanosoma cruzi* and is transmitted from man to man and reservoir animal to man by the reduviid bugs also known as the assassin or the kissing bugs The armadillo opossum rodents dogs and cats are common reservoirs The disease is found chiefly in Central and South America The bugs defecate when they feed and thus contaminate the bite

Pathology The trypanosomes invade the tissue cells of almost any organ in the body and change there to round leishmanial forms The cells become packed with parasites and function is disturbed Replacement fibrosis follows The heart liver and brain are most severely affected

Signs and Symptoms The disease is often mild in adults and severe in children *After an incubation period of about ten days* high fever facial edema adenitis and cardiac weakness set in Death is common especially if meningeal symptoms occur The disease may *become chronic* In such cases the parasites are not found in the blood but exist probably as round forms in tissue cells There are adenitis convulsions nervous disturbances and apathy Anemia and

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means of incision and suction relief of pain and prevention of infection

1 Morphine sulfate 0 01 to 0 016 Gm (1/6 to 1/4 grain) hypodermically is given and the patient made as comfortable as possible

2 A soft rubber tourniquet is applied just above the area of swelling or if there is no swelling just above the bite It should be loose enough so the blood is allowed to flow quite freely but tight enough to occlude the lymphatics so the lymph and venom do not spread

3 Before the patient is moved the area surrounding the bite should be washed with an oxidizing antiseptic to remove the surface venom prophylactic incisions made and suction carried out Procaine anesthesia is used and incisions are made with a sharp pointed blade First the area surrounding the fang marks should be excised Then incisions about one fourth inch in size cross shaped in form are made the knife is inserted and pulled out and if bleeding occurs cotton may be used to plug the incision and another is made nearby Incisions should be staggered at one inch intervals in all directions around the bite and in most cases it is necessary to cover the entire area of swelling There may be 50 to 100 incisions Bier s suction cups or suction apparatus as a breast pump should be applied to the incisions and left there They may be changed from one place to another being left longest on those incisions where the lymph flows most freely Suction may be stopped when lymph no longer appears and hot magnesium sulfate fomentations applied for 45 minutes at the end of which time suction is again applied for 15 minutes and this form is alternated until there is no sign of lymph

4 If the swelling advances the tourniquet should be raised and incisions made as indicated

5 Antitetanus antitoxin 1500 units intramuscularly should be given and repeated in ten days since the tetanus bacillus has been found in the mouths of rattlesnakes Some physicians advise continuing the antitoxin at intervals of eight to ten days if a lacerated wound containing necrotic tissue is present

6 Artificial respiration and respiratory stimulants as aromatic spirits of ammonia 2 cc in a glass of water at intervals of 10 to 15 minutes strychnine sulfate 0 008 to 0 013 Gm (1/8 to 1/5 grain) intramuscularly at 15 minute intervals until slight spasms occur caf

CHAPTER XXIII

Acute Poisoning

SNAKE BITE

Snake venom varies in color from deep amber to a colorless liquid and when dried is quickly soluble in distilled water In general snake venoms are composed of the hematoxin and neurotoxin elements their proportion as well as the toxicity varies in different kinds of snakes They are separable and each may exert its influence individually The hematoxin destroys the red blood cells and tissue and causes severe swelling extravasation of blood discoloration and other signs Neurotoxin attacks the nerve centers, especially the sympathetic system and the phrenic nerve It does not produce swelling but paralyzes the thoracic muscles often to such an extent that the patient suffocates

Signs and Symptoms The onset of symptoms after the bite of a viper is abrupt As stated above swelling and discoloration take place immediately accompanied by oozing of the blood from the mouth conjunctiva bladder and perhaps even from the stomach Reflex vomiting is commonly noted Within 6 to 12 hours the patient may enter a state of coma and die In this type of snake bite it is obvious that the hematoxin element is especially active the blood stream is thinned with hemorrhages over large areas Neutralizing serum or blood transfusions are necessary for the recovery of the patient If he does survive a deep ragged scar will be present from the destruction of the tissue

On the other hand when a person is bitten by the cobra there is slow and moderate swelling and little or no discoloration but great difficulty in breathing is apparent If the patient recovers there is little or no destruction of the tissue at the site of the scar

TREATMENT

The treatment of snake bite may be divided into first aid early local care and the management of late and systemic changes The general treatment is aimed at removing the venom laden lymph by

2 BAL 1 cc of 10 per cent is effectively used in the treatment of arsenic poisoning

3 Freshly prepared ferric hydroxide made by mixing a solution of ferric sulfate 40 cc in 125 cc of water and magnesium oxide 10 Gm (154 grains) in 750 cc of water has always been considered the arsenic antidote but its value is questionable The dose is 15 to 30 cc (½ to 1 ounce) every one to two hours

4 A normal saline colonic irrigation three times a day and guarding against constipation will aid in the elimination of the arsenic since this occurs to a great extent through the feces

5 Since fluid loss is prominent in arsenic poisoning efforts should be directed toward maintaining the composition volume and distribution of extracellular fluids The intravenous administration of 2000 to 3000 cc of five per cent glucose in physiological saline daily will aid in maintaining the body fluid equilibrium Degeneration of the parenchymatous organs as the liver kidneys and heart is combated by intravenous glucose 500 cc of a ten per cent solution twice daily

6 Heat is applied to the abdomen for abdominal cramps and atropine sulfate 0.001 Gm (1/60 grain) hypodermically tincture of belladonna 0.66 cc (10 minims) three times daily and intravenous calcium gluconate 10 cc of a ten per cent solution are given

7 Collapse is treated by the administration of stimulants as caffeine sodium benzoate 0.5 Gm (7½ grains) coramine 2 to 3 cc (30 to 45 minims) or strychnine sulfate 0.001 Gm (1/60 grain) all given intramuscularly and repeated as needed Parenteral fluids and external heat are also indicated

Concerning the use of arsphenamines the two reactions constituting emergencies are the nitritoid crisis and a toxemic reaction The nitritoid crisis is characterized by flushing of the face and neck and a sense of precordial constriction In addition edema of the lids and lips air hunger and collapse may occur The reaction occurs during or a few minutes after the injection Treatment consists of stopping the injection of the drug and giving ½ cc of a 1 1000 solution of adrenalin subcutaneously or intramuscularly and if necessary intravenously The duration of the reaction is from a few minutes to one half hour A few minims of adrenalin given subcutaneously before the injections prevent this reaction

feine sodium benzoate 0 33 Gm (5 grains) *intramuscularly* or caffeine in the form of strong hot black coffee should be given since death from snake bite is most often due to *respiratory paralysis* and failure

7 *If the venom has had time to reach the blood stream* blood transfusions and specific antivenin are usually necessary If the red blood count is below three million blood transfusion is indicated Ten to 15 doses of 10 cc of antivenin may be required but usually 30 cc are adequate for an adult, with more needed for children *It should be injected intramuscularly or subcutaneously into the area* of the bite in severe or late cases it should be given intravenously

ARSENIC POISONING

Arsenic poisoning occurs because of the accidental or intentional ingestion of rat poison or Paris green, and in industry through exposure to oxides of arsenic and arsenical salts Arseniuretted hydrogen is primarily a hemolytic agent Arsenic is a local irritant producing inflammation with sloughing ulceration *and fatty degeneration* Usually within one hour after poisoning there is burning pain in the mouth esophagus and stomach followed by abdominal cramps nausea and vomiting The breath may have a garlic odor A severe diarrhea with rice water and later bloody stools occurs Abdominal distention follows If the patient does not die within a few hours he may die in two or three days from collapse

TREATMENT

1 The immediate treatment is to empty the stomach with emetic drugs such as household mustard 4 to 8 Gm (60 to 120 grains) in a glass of water or copper sulfate 0 5 Gm (7½ grains), or *zinc sulfate* 2 Gm (30 grains) in a glass of water If these fail then apomorphine hydrochloride 0 003 Gm ($1/_{0}$ grain) hypodermically should be given The above drugs should be administered if no stomach tube is available This should be followed by a thorough gastric lavage with water to which may be added 30 Gm (1 ounce) of sodium thiosulfate After the lavage a solution of 30 Gm (1 ounce) of sodium thiosulfate in 500 cc of water is left in the stomach and a similar dose *is repeated daily* *Intravenous injections of* sodium thiosulfate 0 66 Gm (10 grains) should be given daily

The treatment for poisoning from oxalic acid differs from the above in that ordinary alkalies given as an antidote form very soluble salts and thus promote absorption Since calcium and magnesium salts of oxalic acid are insoluble the antidote is 5 to 20 cc of a ten per cent solution of calcium lactate given intravenously slowly There after 10 cc of this solution can be given intramuscularly once or twice daily Calcium chloride 5 to 20 cc of a five per cent solution may be given intravenously if the lactate is not on hand The action must be quick as the poison is rapidly absorbed Calcium gluconate 0 5 Gm (7½ grains) in a glass of milk should be given at three hour intervals To combat the acidosis 6/M solution of sodium lactate as above is given Large amounts of fluid should be given to foster excretion of the acid through the kidneys since nephritis due to renal irritation may develop

ALKALI POISONING

In alkali poisoning there is usually corrosion of the lips mouth throat and esophagus with burning pain down to the stomach The skin is cold and clammy the pulse feeble and usually vomiting and purging and in some cases exhaustion convulsions stupor or coma are present

TREATMENT

1 To combat and neutralize the corrosive action of caustic alkalies weak acids as vinegar lemon or orange juice diluted several times with water are given

2 Soothing demulcents as olive oil milk egg albumen crushed bananas starch or water are given for the burns

3 Morphine sulfate 0 01 to 0 016 Gm (⅙ to ¼ grain) hypodermically is indicated to allay the pain

4 Systemic shock is treated by stimulants parenteral fluids and external heat

5 Stomach tubes should be avoided if strong alkalies have been taken internally because of the weakened esophageal wall

ATROPINE POISONING

Occasionally when used as a medication mild degrees of poisoning with atropine and other members of the belladonna group are

The toxic reaction consisting of nausea and vomiting headache and nervousness is best treated with sodium thiosulfate 1 Gm (15 grains), intravenously daily and alkalinization, using sodium bicarbonate a total of 2 to 4 Gm (30 to 60 grains) being given daily This reaction lasts from two hours to several days The Herxheimer reaction which is an intensification of the constitutional manifestations of syphilis is best prevented by preparation with mercury and bismuth, and an initial small dose of the arsphenamine This is particularly important when cardiac involvement is present

ACID POISONING

The ingestion of strong acids such as sulfuric and nitric produces corrosion of the mouth throat esophagus and stomach The systemic reaction from poisonous amounts is an acidosis resulting in dyspnea twitchings and convulsions collapse coma and finally death

TREATMENT

1 The local reaction should be treated by the oral administration of large quantities of mild alkalies such as milk of magnesia soap or lime water Sodium bicarbonate and other carbonates liberate carbon dioxide gas and will cause marked distention of the stomach

2 Following neutralization of the acid demulcents as olive oil milk egg white or any bland oily substance should be given

3 Stomach tubes should be avoided

4 For the systemic reaction (acidosis) sodium bicarbonate solution (see Acidosis) or 500 cc of a 6/M sodium lactate solution should be given intravenously every hour until the acidosis is controlled

5 Shock and collapse are an indication for supportive treatment consisting of external heat parenteral fluids and stimulants as atropine sulfate 0 001 Gm (1/60 grain) strychnine sulfate 0 002 Gm (1/30 grain) or caffeine sodium benzoate 0 5 Gm (7½ grains) all given intramuscularly Morphine sulfate 0 01 Gm to 0 016 Gm (1/6 to ¼ grain) hypodermically should be administered for pain

6 The symptoms of oxalic acid ingestion are abdominal cramps vomiting and diarrhea due to gastrointestinal irritation and nervous symptoms as a result of calcium depletion characterized by twitchings tetany convulsions coma and death

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ATROPINE POISONING

Occasionally when used as a medication mild degrees of poisoning with atropine and other members of the belladonna group are

seen Dilated pupils tachycardia and palpitation, dryness of the throat thirst and difficulty in swallowing are evidence of overdosage or idiosyncrasy Extremely large doses taken accidentally or with suicidal intentions produce a stage of stimulation followed by col lapse In addition to the above symptoms there are visual disturb ances and excitement which passes into delirium and mania The skin is flushed and the temperature rises very high—41 1° to 42 8 C (106° to 109 F) —and respiration is rapid and deep A stage of col lapse follows characterized by feeble heart action low blood pres sure and slow shallow respiration The skin becomes cold and clammy in contrast to the initial stage of flushing and warmth Death occurs from respiratory failure Urine dropped in a cat s eye at five minute intervals will dilate the pupil

TREATMENT

1 Treatment consists of gastric lavage with tannic acid solution 0 06 Gm (1 grain) in one half glass of water tea or potassium per manganate 1 Gm (15 grains), to a quart of water

2 An ice cap is applied to the head for delirium

3 Sodium bromide in doses of 1 to 2 Gm (15 to 30 grains) is given as needed for excitement

4 Pilocarpine nitrate 0 01 Gm (1/6 grain) is given every few hours until the mouth becomes moist and is considered to be the physiological antidote

5 Because of the tendency to depress respiration morphine chloral and chloroform are to be avoided

6 When collapse occurs intravenous fluids stimulants external heat and artificial respiration should be given

BARBITURATE POISONING

This condition occurs from the ingestion of large amounts of bar bital phenobarbital and other barbiturate derivatives usually with suicidal intent The patient lapses into a deep sleep or coma from which he cannot be aroused Respiration becomes slow and feeble and eventually ceases owing to depression of the respiratory center Collapse occurs with a rapid feeble pulse low blood pressure cyano sis and cold perspiration Pulmonary edema results and later bron chopneumonia may develop The pupils are fixed and constricted

and the deep tendon and abdominal reflexes are diminished or absent Smaller doses of the drug produce unsteadiness giddiness and lethargy

TREATMENT

1 Treatment should begin with gastric lavage after which 30 cc (1 ounce) of magnesium sulfate is left in the stomach

2 Benzedrine 10 to 30 mg orally depending on the result to be obtained may be given

3 Picrotoxin 0 003 Gm (1/20 grain) should be given hypodermically immediately on entrance to the hospital and repeated in 30 minutes If no effect is noted it should be administered every hour until improvement occurs

4 Diuresis is maintained by intravenous fluids as 2000 to 3000 cc of a ten per cent glucose solution or five per cent glucose in normal saline solution

5 Collapse is combated by external heat and atropine sulfate 0 001 Gm (1/60 grain) strychnine sulfate 0 001 Gm (1/60 grain) repeated in one half hour administered intramuscularly caffeine sodium benzoate 0 5 Gm (7½ grains) hypodermically black coffee by mouth ephedrine sulfate 0 05 Gm (¾ grain) orally and coramine 5 cc intravenously repeated at two hour intervals until the patient is aroused

6 The foot of the bed should be elevated and tracheal mucus aspirated

7 If necessary artificial respiration is applied

CARBON MONOXIDE POISONING

Poisoning with carbon monoxide gas usually occurs from accidental or intentional inhalation of illuminating gas or exhaust fumes from an automobile Other sources are defective flues of stoves furnaces charcoal fires or imperfect oxidation of any carboniferous material

Early symptoms before coma occurs are headache dizziness weakness and occasionally nausea and vomiting The lips are often cherry red the face flushed and the skin is usually pale Prolonged exposure to a high concentration produces coma The symptoms are due to asphyxia since hemoglobin has a greater affinity for carbon monoxide than for oxygen Complete elimination of the gas occurs usually in

several hours The outcome however depends upon how long and to what extent the brain has been deprived of oxygen In severe cases coma continues and death occurs even after the elimination of all the carbon monoxide is complete owing to irreparable brain damage

TREATMENT

1 Treatment consists of artificial respiration as needed and the administration of pure oxygen or of oxygen containing five per cent carbon dioxide

2 The patient must be kept warm and the patient should remain absolutely quiet in order that tissue demands for oxygen be kept at a minimum

3 Intravenous sodium bicarbonate four per cent solution 500 to 1000 cc or 500 cc of sixth molar sodium lactate solution should be given to combat the associated acidosis

4 Blood transfusions given within one to two hours after the onset of the poisoning may be of value

5 Methylene blue, 50 cc of one per cent solution intravenously and repeated every hour until 200 cc have been given may be tried but its value is questionable

6 Seriously poisoned individuals should be placed under prolonged observation

COCAINE POISONING

Cocaine and its derivatives cause two types of poisoning The first is sudden and severe and is characterized by irregular jerky respirations rapid thready pulse convulsions and death The second type is more prolonged and begins with mental excitement and loquacity followed by incoordination nausea vomiting abdominal pain and rapid pulse respirations are increased at first and later are slow irregular, and labored Cyanosis delirium and unconsciousness occupy the final stage The pupils are dilated and the extremities cold and clammy

TREATMENT

1 If the cocaine was swallowed gastric lavage with water followed by 2 Gm (30 grains) of tannic acid in one half cup of water or large quantities of strong tea should be given

2 If the stomach tube is not available emetics as apomorphine

0 003 Gm ($\frac{1}{20}$ grain) hypodermically should be given followed by considerable amounts of warm water

3 After the administration of tannic acid the stomach should again be emptied A saline cathartic as magnesium sulfate 30 cc (1 ounce) should be left in the stomach

4 For the treatment of the acute intoxication sodium pheno barbital or sodium amytal 0 33 Gm (5 grains) and paraldehyde 4 cc (1 dram) dissolved in physiological saline are given hypoder mically or even intravenously in severe cases

5 Ephedrine sulfate 0 05 Gm (¾ grain), hypodermically or epinephrine ½ cc in normal saline intravenously is given for col lapse

6 Stimulants as atropine sulfate 0 001 Gm ($\frac{1}{60}$ grain) strych nine sulfate 0 002 Gm ($\frac{1}{30}$ grain) or camphor in oil 1 to 2 cc hypodermically and 30 cc (1 ounce) of whiskey may be given but their actual value is questionable

7 Prophylactic therapy consists of barbital 0 33 Gm (5 grains) by mouth one half hour before and ephedrine sulfate 0 025 Gm (⅜ grain) hypodermically just before the injection of cocaine de rivatives for the purpose of local anesthesia

CYANIDE POISONING

Cyanide poisoning results from ingestion of hydrocyanic acid (prussic acid) from cyanates taken in error or with suicidal intent or from inhalation while fumigating The lethal dose is 0 133 Gm (2½ grains) of cyanate From a large dose death may be instantane ous and the symptoms come on almost with the act of swallowing If hydrocyanic acid has been taken the breath has an odor of bitter almonds Respiration becomes difficult and prolonged the pulse is feeble the pupils are dilated and involuntary urination and defeca tion occur Subsequently convulsions cyanosis paralysis collapse coma and death take place A small dose produces a sensation of weakness and giddiness

If potassium cyanate is taken in addition to the above there are gastrointestinal symptoms due to the drug s caustic action Then nausea and vomiting constriction of the throat and a constricting pain in the chest occur also Confusion of sight and giddiness are common and the patient falls into convulsions

TREATMENT

1 Treatment consists first of maintaining the patient in a horizontal position in the open air, of stimulating respiration with spirits of ammonia and the application of hot and cold water alternately on the chest and spine

2 Artificial respiration is used if indicated

3 If possible, the stomach should be washed with hydrogen peroxide 1 3 dilution or potassium permanganate 1 33 Gm (20 grains) to a pint of water to form a harmless oxamide In addition ferri sulfate 0 66 Gm (10 grains) should be given to form ferri cyanate with hydrogen peroxide used as an oxidizer

4 While the stomach is being washed with potassium permanganate solution an assistant should administer amyl nitrite pearls every three minutes As soon as possible, 10 cc of three per cent sodium nitrite solution is given intravenously followed by 50 cc of a 25 per cent sodium thiosulfate solution If necessary the administration of amyl nitrite pearls is continued again while the sodium thiosulfate is given If the patient survives one half hour the prognosis is fairly good Relapse may occur and consequently the patient should be watched for 48 hours If relapse sets in the above treatment should be repeated using one half the dosages

5 Methylene blue 50 cc of a one per cent solution given intravenously has been considered fairly specific but its actual *value is* still questionable This may be repeated until a total of 200 cc has been given

6 Stimulants as atropine sulfate 0 0006 to 0 001 Gm (1/100 to 1/60 grain) strychnine sulfate 0 002 Gm (1/30 grain) and caffeine sodium benzoate 0 5 Gm (7½ grains) should be given intramuscularly

7 For collapse external heat and intravenous fluids are given

ETHYL ALCOHOL POISONING

Ethyl alcohol poisoning brought on by the consumption of alcoholic beverages is commonly known as drunkenness and in its final stages resembles complete anesthesia The patient is at first hilarious with a thick speech and uncertain gait associated with varying degrees of emotional instability as pugnacity remorsefulness and lethargy Further poisoning results in coma and at times collapse

TREATMENT

1 If the stage of complete coma is not present the patient should be allowed to sleep it off

2 The stomach should be emptied by lavage so the alcohol will not be absorbed

3 In addition black coffee and fresh air should be provided

4 The patient must be kept warm and adequately covered

5 If he is in coma and collapse external heat and stimulation with atropine sulfate 0 0008 Gm (1/80 grain) strychnine sulfate 0 002 Gm (1/30 grain) or caffeine sodium benzoate 0 5 Gm (7½ grains) all given intramuscularly should be administered Carbon dioxide oxygen inhalations should be administered Intravenous fluid in the form of 50 cc of 50 per cent glucose may be administered

6 The stage of excitement is controlled by the oral administration of chloral hydrate and sodium bromide 2 Gm (30 grains) of each or paraldehyde 4 to 12 Gm (1 to 3 drams)

7 When the patient regains consciousness the hangover should be treated with a saline purge tea milk and toast as tolerated and aspirin 0 33 Gm (5 grains) with caffeine citrate 0 1 Gm (1½ grains) for the headache

METHYL ALCOHOL

Methyl or wood alcohol poisoning results usually from the ingestion of denatured alcohol and anti freeze mixtures used in automobiles Since the repeal of prohibition the number of cases has decreased but occasionally through ignorance this substance is used as a beverage during drinking bouts Poisoning can also occur through the inhalation of the fumes as when methyl alcohol is used in industry The symptoms develop in a few hours to a few days and the onset is usually characterized by marked vomiting and abdominal pain headache dizziness and stupor Later profound collapse and delirium develop with dyspnea cyanosis rapid weak pulse and dilated irregular pupils Depression of the heart and voluntary muscle results Disturbance of vision often resulting in blindness is characteristic

TREATMENT

1 Treatment consists of frequent gastric lavage with four per cent sodium bicarbonate solution and the introduction of some of

this solution into the rectum After the lavage an ounce of magnesium sulfate should be left in the stomach At times it may be necessary to administer apomorphine hydrochloride 0 006 Gm (1/10 grain) The lavage should be followed by an injection of morphine sulfate 0 016 Gm (1/4 grain), hypodermically in order to lessen the suffering If the patient is wild hyoscine 0 0002 Gm to 0 0003 (1/300 to 1/200 grain), should also be given

2 The acidosis may be combated by the administration of several hundred cubic centimeters of a sixth molar sodium lactate solution intravenously four or five times a day

3 The patient should be kept warm and his nutrition maintained

4 Collapse is treated with external heat and stimulants, as strychnine sulfate, 0 002 Gm (1/30 grain) atropine sulfate 0 001 Gm (1/60 grain) caffeine sodium benzoate 0 5 Gm (7½ grains) and camphor in oil 2 cc (30 minims) intramuscularly

5 Drainage of the spinal fluid may help avoid blindness

IODINE POISONING

Iodine is usually taken in the form of tincture it may be mistaken for some other medicine or taken with suicidal intentions As a rule *the only result of its ingestion is stomatitis and perhaps gastritis* On occasions if treatment is not administered soon enough or if large quantities have been ingested severe gastroenteritis with nausea and vomiting develop The patient becomes pale giddy and faint and the pulse is rapid and feeble A high fever and suppression of urine may occur At times the eyelids become swollen and albuminuria may occur Cyanosis and great excitement with convulsions followed by collapse may result

TREATMENT

1 A solution of starch should be given and the stomach evacuated with a stomach tube as soon as possible Lavage should be done with large quantities of water containing egg and starch

2 This should be followed by administration of demulcents as white of egg milk and bland oils

3 In case of collapse stimulants as brandy or whiskey 30 cc (1 ounce) or aromatic spirits of ammonia 2 to 4 cc (30 to 60 minims) may be given

4 Strychnine sulfate 0 001 Gm (1/60 grain) every two hours atropine sulfate 0 0006 to 0 001 Gm (1/100 to 1/60 grain) every two hours and caffeine citrate 0 24 Gm (4 grains) every hour should be given hypodermically

5 Collapse also requires external heat and intravenous fluids

6 Administration of morphine sulfate 0 016 Gm (1/4 grain) hypodermically is a means of relieving pain and symptoms of apprehension

MERCURIC BICHLORIDE POISONING

Mercuric bichloride typifies severe mercury poison and because of its availability poisoning is not rare Death occurs from taking one 0 5 Gm (7½ grains) tablet Ingestion of strong solutions causes corrosion of the mouth pharynx esophagus and stomach Early symptoms are abdominal cramps and vomiting often of blood Later inflammation and necrosis of the colon and upper rectum and degeneration of the convoluted tubules of the kidney occur The patient then dies of a severe colitis with a bloody diarrhea and an anuria resulting in uremia

TREATMENT

1 The immediate treatment is to remove as much of the mercury from the stomach as possible A glass of milk and a glass of egg albumen are given followed by gastric lavage to remove the albuminate formed with the mercury

2 On admission to the hospital a second lavage is done and a pint of milk is left in the stomach

3 The following treatment is then continued until no mercury is found in the urine on two successive days

a The patient is given 240 cc (8 ounces) of milk every two hours and on the alternate hour 240 cc (8 ounces) of a mixture of 4 Gm (1 dram) potassium bitartrate 4 Gm (1 dram) sugar 15 cc (½ ounce) lactose 30 cc. (1 ounce) lemon juice and boiled water to make one pint.

b Continuous rectal drip administration of a solution of potassium acetate 4 Gm (1 dram) to 500 cc. (1 pint) of water It is important to carry on this treatment continuously especially between the fifth and tenth days at this time there is a decrease in the amount of urine secreted If the patient passes this stage of the poisoning successfully the secretion of urine usually increases often to high levels.

this solution into the rectum After the lavage an ounce of magnesium sulfate should be left in the stomach At times it may be necessary to administer apomorphine hydrochloride 0 006 Gm (1/10 grain) The lavage should be followed by an injection of morphine sulfate 0 016 Gm (1/4 grain), hypodermically in order to lessen the suffering If the patient is wild hyoscine 0 0002 Gm to 0 0003 (1/300 to 1/200 grain), should also be given

2 The acidosis may be combated by the administration of several hundred cubic centimeters of a sixth molar sodium lactate solution intravenously four or five times a day

3 The patient should be kept warm and his nutrition maintained

4 Collapse is treated with external heat and stimulants as strychnine sulfate 0 002 Gm (1/30 grain) atropine sulfate 0 001 Gm (1/60 grain) caffeine sodium benzoate 0 5 Gm (7½ grains) and camphor in oil 2 cc (30 minims) intramuscularly

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c Gastric lavage twice a day
d Colonic irrigation twice a day
e Hot pack sweat twice a day
f Intravenous injections of sodium thiosulfate 1 Gm (15 grains) in 10 cc of aqueous solution twice daily In severe cases a total of 6 Gm (90 grains) daily for three to five days should be given
g Caffeine sodium benzoate 0 2 to 0 33 Gm (3 to 5 grains) strychnine sulfate 0 002 Gm (1⁄30 grain) atropine sulfate 0 0008 Gm (1⁄75 grain) all administered hypodermically external heat and intravenous five per cent glucose in physiological saline solution in amounts of 1000 to 3000 cc should be given for collapse
h For pain morphine sulfate 0 016 Gm (1⁄4 grain) hypodermically
i Decapsulation of the kidney should be considered when anuria persists for two or three days
j Sodium formaldehyde sulfoxylate 500 to 1000 cc of a five per cent solution has been suggested but this form of therapy does not seem to produce any better results than other measures It must be given immediately (within one hour) to be of any value A five per cent solution is used for gastric lavage after which 200 cc. of the solution are left in the stomach An intravenous injection is then given 10 Gm (150 grains) dissolved in 100 to 200 cc of fluid being infused over a 20 minute period The sulfoxylate may thus come in contact with the *mercury bichloride and convert it into an insoluble mercurous compound*

MORPHINE POISONING

Morphine poisoning occurs from either the therapeutic use of too large a dose of the drug or from injection for suicidal purposes Mild cases show lethargy from which the patient can be aroused constriction of the pupils slow respiration and occasionally nausea and vomiting Large doses produce marked stupor Cheyne Stokes respiration pin point pupils cyanosis and warm flushed skin The pulse is slow and regular and of fairly good quality Still larger doses produce marked coma collapse cold clammy cyanotic skin and marked slowing and irregularity of respiration with long periods of apnea

TREATMENT

1 The treatment in mild cases consists of keeping the patient awake and in fresh air and giving caffeine sodium benzoate *0 5 Gm* (7½ grains) intramuscularly every four to six hours

2 In the more severe cases when the drug has been taken by mouth the stomach should be washed several times with a solution

of potassium permanganate 1 Gm (15 grains) to a quart of water

3 Frequent colonic irrigations aid in removing the morphine as it is excreted

4 If the patient can be aroused at all he should be kept awake by annoyance with some form of external activity and even walked about if possible This should be continued ceaselessly until the patient is out of danger

5 Caffeine sodium benzoate 0 33 Gm (5 grains) hypodermically black coffee orally and per rectum and ephedrine sulfate 0 025 to 0 05 Gm (3/8 to 3/4 grain) orally should be administered every hour if necessary to stimulate respiration

6 If the patient is in a state of coma and collapse from which he cannot be aroused the treatment is external heat oxygen and carbon dioxide inhalations caffeine and ephedrine as above

7 Artificial respiration must be employed if the natural process ceases

PHENOL POISONING

Phenol poisoning is characterized locally by the odor and by corrosion of the mouth and tongue with the formation of a white eschar Systemically phenol is a depressant of the central nervous and circulatory systems Large doses cause collapse and unconsciousness with muscular twitchings and rarely convulsions followed by death in a few hours from respiratory failure More dilute solutions cause a more gradual onset of collapse from depression of the vasoconstrictor and respiratory centers The patient becomes weak dizzy and is mentally depressed The common findings are a rapid thready pulse lowered blood pressure pallor or cyanosis and a cold clammy skin Recovery or coma follows Later manifestations are ulceration of the mucosa of the stomach with cicatrization and nephritis

TREATMENT

1 Gastric lavage should be carried out with caution After copious amounts have been used a portion of the oil should be left in the stomach to act as a diluent and demulcent

2 The patient should be kept warm

3 Any systemic reaction is treated with respiratory and circulatory stimulants as caffeine sodium benzoate 0 13 to 0 33 Gm (2 to

5 grains) atropine sulfate 0 0008 Gm (1/[illegible] grain) strychnine sulfate 0 002 Gm (1/30 grain), and epinephrine ½ cc of a 1 1000 solution all given hypodermically

4 Hypertonic solutions as 50 cc of a 50 per cent glucose solution are given intravenously for pulmonary edema

5 Oxygen should be given in case of collapse and cyanosis

PHOSPHORUS POISONING

Yellow phosphorus is poisonous and is present in rat poison and some old style matches Red phosphorus is nonpoisonous and is used on the box of safety matches and for the ends of some other types The rat poison in addition to containing yellow phosphorus may also contain arsenic and strychnine The symptoms of acute poisoning usually occur after a period of three to four hours There is a phosphorus or garlic odor to the breath with nausea and vomiting of mucus bile and blood The vomitus is luminous in the dark Burning pain in the esophagus and abdomen due to inflammation of the gastrointestinal tract is present There may be diarrhea and bloody stools Jaundice associated with a large tender liver may develop The abdomen becomes distended The patient complains of headache and dizziness The urine is scanty and contains albumin Delirium convulsions and coma may occur Death may result in 24 to 48 hours from respiratory paralysis or degeneration of the liver and kidney Autopsy shows a fatty degeneration of the kidneys liver and heart

TREATMENT

1 The immediate treatment is to wash the stomach with water to which 1 teaspoonful of old oil of turpentine has been added

2 If no stomach tube is available copper sulfate 0 33 Gm (5 grains) in 30 cc (1 ounce) of water should be given every five to ten minutes until vomiting occurs The copper sulfate forms an insoluble and nontoxic copper phosphide Zinc sulfate can be used in a dose of 1 33 Gm to 30 cc (20 grains to 1 ounce) of water

3 Oils and fats and substances containing fats should be avoided as they increase the solubility and absorption of the phosphorus Liquid petrolatum owing to its inert qualities may be given immediately after the ingestion of the phosphorus followed by a lavage

Petrolatum is used only in case oil of turpentine and copper sulfate are not readily available

4 After the stomach has been washed the patient should be given old oil of turpentine ½ teaspoonful in warm water or capsules every 15 to 30 minutes This forms an insoluble mass with the phosphorus

5 Potassium permanganate solution 1 1000 or one per cent hydrogen peroxide solution may be used for lavage instead of the above mentioned method

6 Magnesium sulfate 30 Gm (1 ounce) in water should be given following the above treatment

7 Hot abdominal stupes intravenous glucose solution 2000 3000 cc of a five per cent glucose in physiological saline daily with insulin and calcium salts as calcium lactate or calcium gluconate in amounts of 1 Gm (15 grains) three times a day should be administered to protect the liver

STRYCHNINE POISONING

Strychnine poisoning occurs from absorption of strychnine nux vomica and brucine In a mild form it may be a result of therapeutic overdosage The patient appears restless and exhibits twitching of fingers or jerking motions of the arm or leg Some stiffness of the face (rarely) fingers or gait may be present Withdrawal of the drug and the administration of bromides or barbiturates will relieve the symptoms In severe poisoning a generalized convulsion involving all muscles is present The position of the patient during the convulsion is in opisthotonos The action of all the extensor muscles of the body predominates During the convulsion there is a marked cramp like pain in the muscles The mind is clear and therefore the suffering is great

TREATMENT

1 The first step in the treatment is the administration of a rapidly acting barbiturate Sodium amytal 0 4 to 1 Gm (6 to 15 grains) in 10 cc of sterile water is administered intravenously slowly and may be repeated if necessary The dosage cannot be stated dogmatically but the drug should be given in amounts large enough to control or antagonize convulsions and keep the patient asleep yet not so great as to depress respiration and blood pressure Chloroform inhalations may be given to control convulsions until a barbiturate

can be given Prolonged ether or avertin anesthesia may be administered for a period of five or six hours

2 If there is a possibility that some of the drug is in the stomach after the convulsions are controlled gastric lavage using a 1 1000 concentration of potassium permanganate solution is indicated or one may administer 1 teaspoonful of tannic acid in one half glass of hot water or 15 drops of tincture of iodine in one half glass of water

3 The patient should be kept in a dark quiet room

4 Bromides in the form of sodium bromide 15 Gm (225 grains) by mouth or rectum are beneficial, since they are antagonistic to strychnine in their action on the cord The bromides may be administered as an adjunct to the barbiturates However the patient must be closely observed so that sedatives are not given to the point of respiratory depression

5 Intravenous physiological saline 3000 to 4000 cc daily should be given to establish free diuresis and to aid in the elimination of the drug The patient should be catheterized frequently to prevent reabsorption of the excreted strychnine

6 Inhalations of oxygen are indicated to aid oxidation of the strychnine

7 Artificial respiration is used as needed

8 Stimulants as atropine sulfate 0 001 Gm (1/60 grain) and caffeine sodium benzoate 0 2 Gm (3 grains) should be administered when necessary

FOOD POISONING

Contaminated food may cause poisoning characterized chiefly by gastrointestinal symptoms which may be mild or severe The severe kind may be fatal especially in babies youngsters and in older debilitated individuals Canned food of any kind salmon sausage tomatoes fruits and milk may carry the disturbing toxins or organisms Custards and pastries such as chocolate eclairs are excellent culture media for the germ and are often causes of food poisoning The term ptomaine poisoning is not usually appropriate for this kind of disease because it is usually the group of organisms of salmonella which is the responsible agent The ptomaines themselves are not the cause of the food poisoning the real cause is bacteria Foods in hot climates and in warm periods of the year in any climate

must always be watched closely for slightest evidence of putrefaction inasmuch as most of these epidemics occur in the summer

A period of from 2 to 48 hours elapses after the ingestion of the food before symptoms of intoxication develop usually the period of incubation is about six hours There is an explosive onset of signs and symptoms with violent nausea and vomiting severe diarrhea abdominal cramps and evidence of prostration Fever exceeds 37 8° C (100 F) the patient rapidly becomes dehydrated and signs of dehydration are added to those of intoxication Circulatory collapse may ensue The diagnosis is usually easy especially when it is determined by the history that more than one person eating at the same table became ill Other conditions as mesenteric thrombosis embolism acute appendicitis acute pancreatitis and ulcerative colitis may simulate the gastroenterocolitis of food poisoning

TREATMENT

1 On reaching the patient s bedside all foods that have been partially eaten should be collected for examination The vomited material too should be taken to a laboratory for bacteriological examination and identification of the organism

2 The stomach should be washed out with saline solution and kept up until all the contents of the stomach have been removed The bowels should be thoroughly evacuated as soon as possible If there has not been a free bowel movement after the stomach has been cleaned out magnesium sulfate 15 Gm (½ ounce) should be given cleansing the lower bowel with a plain water enema is often of benefit

3 An intravenous administration of 1500 to 2000 cc of normal saline solution should be started immediately and repeated every eight hours to combat dehydration

4 A hypodermic injection of dilaudid 0 002 Gm (1/24 grain) is often sufficient to overcome the severe cramps Hot stupes are of benefit

5 If the patient is able to take drugs by mouth one teaspoonful of paregoric in warm water repeated every four hours is beneficial or a teaspoonful of a preparation containing 16 Gm (4 drams) of tincture of belladonna and 120 Gm (4 ounces) of elixir of phenobarbital may be given every three hours to obtain sedation of the patient in general and of the bowels in particular

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surfaces by children but the majority develop from occupational contact with lead in some form

When painters metal finishers sprayers or other lead workers do not cleanse their hands carefully before eating they may swallow lead with their food However the alimentary tract is the least dangerous avenue for the entrance of lead since most of the lead absorbed goes to the liver where there is a barrier which it must go through to reach the other internal organs Consequently most of the lead taken by mouth is filtered by the liver and there are no ill effects

The lung is the most dangerous path of entry Since there is no protective barrier the lead is absorbed directly into the circulation of the lung carried to the heart and distributed to the essential internal organs the brain kidneys liver muscles and nervous system

When lead is absorbed into the body by any of these routes it is deposited in the bones It forms a chemical combination with calcium the calcium is deposited in the bones and the lead becomes inert As times goes on the deposited lead may be released from the bones and enter the blood stream thereby producing acute lead poisoning after the initial exposure Lead in the bones is always a potential source of an acute attack of lead poisoning

Signs and Symptoms Lead absorption is characterized by the presence of lead in the stools and a lead line on the gums This lead line is not found in the absence of teeth or in a completely healthy mouth otherwise it is usually present on the buccal rather than the labia aspect of the gums and most often around the molars The four principal signs of lead poisoning are colic anemia palsy and lead line

In acute lead poisoning that occurring after short but severe exposure the onset consists of sudden illness with marked weakness severe colic nausea and vomiting with or without constipation The picture resembles acute intestinal obstruction or some acute abdominal condition which is ruled out by the normal pulse temperature and leukocyte count and the history of lead exposure or lead in the urine In the more chronic type the patient becomes ill gradually There is a history of loss of appetite and weight weakness lassitude mental depression constipation and attacks of mild abdominal distress Perhaps the first cause for complaint is wrist drop or some loss of functions of the hands or arms Lead poisoning may bring about

6 If the patient has gone into an episode of serious vascular collapse external heat must be applied and caffeine sodium benzoate 0 24 Gm (4 grains) may be given intramuscularly Occasionally oxygen is indicated Within a period of 12 hours patients usually recover

MUSHROOM POISONING

TREATMENT

Treatment consists in gastric lavage with warm water as soon as possible and the administration of atropine sulfate 0 001 Gm (1/60 grain) intramuscularly At times the patient is greatly depressed and coramine 5 cc intramuscularly may be given It is wise also to administer 1000 cc of ten per cent glucose in normal saline intravenously Transfusion may be necessary Administration of freshly chopped brains and stomachs of several rabbits by mouth is said to produce a combination with the toxin and act as a specific

There are two main types of mushroom poisoning In one the symptoms are largely those of gastroenteritis In the second and more fatal type the symptoms and findings are largely those of injury to the nervous system with headache somnolence trismus mydriasis sometimes opisthotonos with other forms of muscle cramps at times blindness loud cries and ultimately coma The symptoms commonly appear four to five hours after the meal Atropine sulfate is a specific in treatment of the latter type and should be given until the physiological effect is produced

LEAD POISONING

Lead poisoning is one of the most important industrial diseases It most frequently occurs among workers exposed to lead However it must be emphasized that many people who are exposed to lead do not absorb it lead poisoning only occurs when lead is absorbed over a considerable period of time True acute lead poisoning is quite rare since it usually develops after the sudden intake of large doses of lead as those taken with suicidal intent It is this type as well as the acute exacerbation of the chronic type that a physician is called on to treat

Etiology Lead may enter the body through the gastrointestinal tract the respiratory tract or even through the skin Some cases have resulted from the use of hair dyes cosmetics or ingestion of painted

CHAPTER XXIV

Drugs

DRUGS USED IN THE TREATMENT OF HEART DISEASE

When we speak of the drug treatment of heart disease and heart failure we may classify the drugs into three classes

1 Drugs that affect the heart directly
   a Digitalis
   b Quinidine
   c Squills
   d Strophanthin
2 Drugs that are adjuncts to therapy These drugs called diuretics do not help the heart directly
   a Xanthines as theobromine which increase the flow of urine
   b Mercurials as salyrgan which work on the tubules of the kidneys
   c Acid forming salts as ammonium chloride which work out in the cells of the body affecting the electrolyte responses
3 Soporifics or sedatives which are important aids in treatment
   a Barbiturates.
   b Bromides
   c Opium alkaloids
   d Chloral hydrate and miscellaneous agents

Digitalis Of all the drugs used in the treatment of heart disease digitalis is the most reliable and trustworthy No other drug requires more experience skill and care in administration Gastrointestinal disturbances bradycardia cerebral symptoms and skin manifestations may develop in the course of digitalis therapy but careful administration will usually avert these complications The disappointments attending the use of digitalis arise not so much from toxic manifestations as from its use in cases where it is contraindicated and from underdosage

For an understanding of the clinical use of digitalis its pharmacological action must be considered This may be summarized as follows (1) It slows the heart rate by virtue of its depressing action on the sinoauricular and auriculoventricular nodes (2) It acts upon the muscle of the auricles and ventricles and retards the conduction

injury to almost any organ of the body There may be lead encephalitis lead nephritis or lead arteriosclerosis

The blood picture usually reveals early evidence of lead poisoning The characteristic feature of the anemia is that the count seldom drops below three million *There is marked destruction of erythrocytes* with an increase in red cells Stippled cells appear blood study showing 100 stipplings to 1 000 000 red cells though the stipplings have ceased to be looked on as an outstanding diagnostic feature because so many patients with idiopathic anemias of other types show it

Another important diagnostic feature is the appearance of lead in the urine which points to lead intoxication this is not true of lead in the feces

TREATMENT

1 The main object of the treatment of acute lead poisoning is to immobilize the lead in the blood stream This is accomplished by giving large doses of calcium by mouth or vein since it combines with the lead and both are deposited in the bone

2 A nutritious diet should be given A milk diet or 6 to 8 Gm of calcium added to one or two quarts of milk aids in the immobilization of lead

3 The colic may be relieved by intravenous calcium *gluconate* atropine nitroglycerin or the application of heat

4 A saline cathartic or enema may be given if the diagnosis is certain it will increase the elimination of lead

5 Large doses of iron should be given

6 Sodium citrate 4 Gm (60 grains) in one ounce of water three times daily or for severe cases 50 cc of a sterile 2 5 per cent aqueous sodium citrate solution intravenously relieves symptoms

7 After the acute episode is passed the process of deleading should be started The hydrogen ion concentration of the blood is slightly increased by the administration of large doses of ammonium chloride 3 3 Gm (50 grains) three or four times a day Sometimes potassium iodide will assist in the liberation of lead from the system By slightly increasing the hydrogen ion concentration the lead is delivered up to the blood stream and excreted in the urine and feces Thus small amounts of lead are given off from the deposits and acute episodes of lead poisoning will not occur

and because effective action is difficult to obtain this way For rapid digitalization which is rarely required 0 2 Gm (3 grains) (two tablets pills capsules or 2 cc of the tincture) may be given orally four times a day for two or three days In case of emergency 0 5 Gm (7½ grains) in solution such as 10 cc of digifoline or some other preparation may be given intravenously and repeated two or three times a day for several doses

Contraindications It is as important to know when digitalis should not be given as when it is indicated In brief the conditions in which digitalis is sometimes used but may actually be harmful are as follows (1) The tachycardia following operations and postoperative infections (2) the rapid heart of acute infectious disorders such as pneumonia (3) coronary thrombosis (4) extrasystoles (5) tachycardia of hyperthyroidism (6) paroxysmal tachycardia and (7) heart block Although the drug may be administered to patients who are arteriosclerotic digitalis must be given to older people with considerable caution Also digitalis does not combine well with certain other drugs For example it must not be given to a patient who is taking calcium epinephrine ephedrine or atropine

It is important that a patient taking digitalis be examined frequently in order to avoid overdosage The results of overdosage may be summarized as follows (a) There may be nausea vomiting or diarrhea (b) The heart may be slow and coupling of the beats may occur (c) There may be cerebral symptoms such as headache delirium depression confusion or visual disturbances Omission of digitalis for two days usually clears up these unfavorable reactions and the drug may then be given again in smaller doses for a period of a few days

Recently extracts of digitalis lanata (yellow digitalis) have been used in cases where digitalis purpurea caused nausea vomiting or intoxication They are administered in doses of 0 1 Gm (1½ grains) as is digitalis purpurea

The Cardiac Glycosides Within recent years special attention has been devoted to the pure cardiac glycosides The introduction of the purified cardiac principles has brought some changes in the use of digitalis clinically and has broadened the therapeutic possibilities of digitalis Of the numerous glycosides of digitalis available some have gained greater popularity than others There are three

through the auriculoventricular bundle of His (3) It increases the tonicity and the contractile power of the heart muscle resulting in a more complete contraction of the ventricles and more effective emptying of the chambers This leads to a greater cardiac output and improvement of the circulation

Indications There are three possibly four main indications for the use of digitalis (a) Congestive heart failure associated with auricular fibrillation The results of digitalis therapy are most outstanding in this condition (b) Congestive heart failure with normal rhythm Here the effects of digitalis are desirable but they are not as dramatic as when fibrillation exists (c) Auricular flutter In these cases digitalis converts the flutter into fibrillation which it controls satisfactorily (d) Hypertensive heart disease Some authorities believe that small doses of digitalis given before heart failure begins prevent further dilatation and hypertrophy and forestall heart failure

Methods of Administration and Dosage Digitalis is most commonly prescribed in tablet pill powdered leaf in capsule or in the tincture forms These preparations are standardized so that one tablet one pill one capsule and 1 cc of the tincture each represent one cat unit which is the American unit of the potency of the drug A cat unit is that amount of the drug calculated per kilogram of cat which is just sufficient to kill slowly and continuously when injected into the vein It does not make much difference which preparation is used for in most cases the digitalis effect is obtained from any one of them Occasionally it is found that a patient responds better to one form than another and the tolerance to the drug varies in different individuals

As a general rule the drug should be given in sufficient doses to obtain the desired effect as soon as possible This is accomplished best by giving one cat unit four to six times a day Although other methods have been advocated none is superior to the oral administration of ordinary doses at frequent intervals throughout the day Digitalis should be given until the therapeutic effect has been obtained and then the daily maintenance dose should be adjusted to the individual patient to maintain the optimum digitalis effect

Digitalis may be given intramuscularly but this is to be discouraged as much as possible because of the pain caused by the injection

DOSAGE OF CARDIAC GLYCOSIDES

Glycoside	Digitalizing Dose		Daily Maintenance Dose (oral)
	Oral	Intravenous	
Cedilanid (Sandoz)	6.0 mg in 48 hrs 7.5 mg in 72 hrs	1.6 mg or 1.2 mg followed by 0.4 mg in 2-4 hrs	0.5-2.0 mg (Average 1.5 mg)
Digilanid (Sandoz)	4.0-8.0 mg in 24-48 hrs (Average 6.0 mg)	3.0-6.0 mg	[illegible] mg
Digitoxin (Abbott)	1.0-1.5 mg	1.0-1.25 mg	0.1-0.2 mg
Digoxin (Burroughs-Wellcome)	1.0-1.5 mg	0.75-1.0 mg	0.5 mg
G-Strophanthin (Ouabain) (Lilly)		0.5 mg (Initial dose of 0.25mg repeated in 2 hrs)	
K-Strophanthin (Abbott, Burroughs-Wellcome)		0.5-0.75 mg (Initial dose of 0.3-0.5 mg followed by 0.5 mg in 6 hrs	
Scillaren (Sandoz)	9.6-14.4 mg in 72 hrs		0.8-1.6 mg
Urginin (Lederle)	6.5-14.0 mg in 72 hrs (Average 9.0 mg)		0.5-1.5 mg (Average 0.95 mg)

Quinidine is not as widely used as digitalis because sometimes it results in embolism and death It is a protoplasmic poison It may be used advantageously in

1 Young individuals with auricular fibrillation it is not a drug for the treatment of heart failure but only for fibrillation in young people

2 Post thyroidectomy cases with auricular fibrillation

3 Patients who are not helped by digitalis

Quinidine is a destroyer of the heart muscle so it should not be used over a long period of time It slows the impulses of the heart coming down from the auricle through the A V node to the ventricle It acts as a depressant

Quinidine sulfate is usually used It is a bitter white crystalline powder fairly insoluble in water and is usually prescribed in capsules of 0.2 to 0.5 Gm (3 to 7½ grains) Both quinidine and digitalis slow auricular impulse conduction and lengthen the refractory period but since quinidine depresses restorative metabolism it is used for the arrhythmia to restore the disorder to normal Quinidine has almost the same toxic effects as quinine *It may produce cinchonism*

chemically pure substances known as lanatoside A B and C which may be isolated from digitalis lanata Of these lanatoside C is considered most valuable therapeutically Cedilanid is a synonym for lanatoside C and digoxin is another pure glycoside closely related to lanatoside C These newer and more popular glycosides of digitalis lanata have the same fundamental action upon the heart as the glycosides of digitalis purpurea

Some distinct advantages of lanatoside C over the older digitalis preparations are apparent (1) The method of standardization makes unnecessary the need for bio assay and the potency of the pure glycosides is not variable (2) lanatoside C is easily absorbed and its action is prompt (3) the gastrointestinal disturbances nausea vomiting and diarrhea are less frequently observed with the purified glycosides (4) when rapid digitalization by the intravenous method is desired the pure glycosides are preferred Intravenous and intramuscular injections also are satisfactory when digitalis cannot be given by mouth (5) the purified glycosides may have toxic actions just as the preparation of the powdered leaf exert *The glycosides* of digitalis purpurea and digitalis lanata are chemically closely related (6) the use of the pure glycosides does not obviate the necessity for knowledge skill and experience on the part of the physician prescribing them

Regarding the problem of using the ordinary digitalis or the pure glycosides the following statement may be made The patient may *be treated satisfactorily with any one of the standard preparations* but the older preparations are more variable in potency than the pure glycosides The individual reactions of the patient to one or the other preparations of digitalis is and always will be an unknown factor until the drug is employed Therefore while it is wise to know about the many preparations of digitalis on the market it is most desirable to become thoroughly familiar with a few of them In the choice of digitalis preparation (1) Potency (2) absorbability (3) speed of action and (4) speed of elimination must be considered Some of the pure glycosides possess these features more completely than any of the older forms

The following table on *the Dosage of Cardiac Glycosides* is taken from *Digitalis and other Cardiotonic Drugs* by Eli Rodin Movitt Oxford University Press New York 1946

Drugs that are adjuncts to therapy

Xanthines This group is composed of caffeine theobromine and theophylline and their salts They act on the kidneys stimulate the central nervous system and myocardium and dilate the coronary vessels Caffeine is not used very much because it acts as a stimulant on the brain Theobromine is given in doses of 0 6 Gm (10 grains) orally three or four times a day for four or five days theophylline is administered in doses of 0 3 Gm (5 grains) on the same routine The salts of these drugs which include theobromine sodium salicylate theobromine sodium acetate theocalcin theophylline sodium acetate theophylline calcium salicylate and theophylline ethylenediamine are given in oral doses of 0 5 Gm (7½ grains) three or four times daily The salts usually cause nausea and vomiting

These drugs tend to raise the blood pressure by central vasomotor stimulation but they cause the blood pressure to fall by the peripheral action on blood vessels When the patient has cardiovascular disease caffeine cannot be used because of its stimulation of the nervous system The other two xanthines are usually used in angina pectoris and are best given at mealtime to lessen gastric irritation Best results are obtained when they are used in conjunction with sedatives or nitrites Theophylline is often used to bring relief in cases of paroxysmal cardiac dyspnea and cardiac asthma

The most commonly used *mercurials* are salyrgan mercupurin mercuhydrin and mercuzanthin They are the most potent diuretics diuresis starts in two or three hours and is over in about ten hours Nearly all of the injected mercury is excreted by the kidneys The diuretic action of the mercurials seems to be renal

Novasurol though it produces profound diuresis seems to cause toxic reactions in some people and for this reason less toxic organic salts are usually used Merbaphen (novasurol) is used with hesitancy in cases of noncardiac edema because it produces certain irritation as stomatitis vomiting proctitis bloody diarrhea as well as a decrease in urinary output and showers of casts and red blood cells

Salyrgan theophylline a nonirritating mercurial is a 10 per cent solution of mercury salicylallylamide o-acetate of sodium The initial dose of 0 5 cc (7½ minims) intravenously is raised to 1 5 or 2 cc (22½ or 30 minims) once or twice a week This may be increased to 3 cc (45 minims) one to three times a week depending on the results

nausea and vomiting respiratory distress giddiness cyanosis and cold perspiration Other unfavorable results are ventricular fibrilla tion and standstill embolism or increased ventricular rate

Before starting quinindine administration the patient should have complete bed rest and sedation Digitalis should be given and treatment completed in all patients with ventricular rates over 90 beats per minute to forestall dangerous tachycardia It is usually best to give a test dose of 0 2 to 0 3 Gm (3 to 4½ grains) of quinidine to see how it reacts and if there are no unsatisfactory re sults a course of treatment of 0 4 Gm (6 grains) every four hours or five times daily should be given for a period of about one week If there are toxic effects tachycardia over 125 beats per minute ob stinate flutter or if normal rhythm is not restored by the tenth day administration should be discontinued Then two weeks later treat ment may be started again If normal rhythm is restored a dose of 0 2 to 0 3 Gm (3 to 4½ grains) of quinidine should be given three times daily for a short time and then gradually omitted

Quinidine should not be used on patients with acute infections or vegetative endocarditis advanced organic change in the myocar dium without heart failure long standing auricular fibrillation or chronic valvular disease complete heart block embolic phenomena when the heart is seriously damaged or in elderly patients

Squills as such are obsolete A squill is a sea onion belonging to the lily family Its glycosidal fractions are in the form of urginin scillaren and scillaren B

Strophanthin Ouabain is a crystalline glycoside from strophan thus which contains digitalis like drugs It is not usually used by phy sicians since digitalis is preferred Strophanthus tincture causes diar rhea and since it varies in potency and is often poorly absorbed by the intestinal tract poisoning is apt to result Ouabain and amor phous k strophanthin B (strophanthin) are sometimes used paren terally Strophanthin is usually given in 0 0006 Gm (1/100 grain) doses for quick action on patients with fibrillation and failure Most physicians recommend 0 0006 Gm (1/100 grain) once a day but I prefer to give it twice a day although many feel it sometimes results in nausea vomiting and irrationality It must be emphasized that digi talis must not have been used for at least five days before beginning the use of strophanthin otherwise the heart will stop in systole

divided doses of 8 to 12 Gm (120 to 180 grains) daily This dosage will start or continue diuresis and relative acidosis Other diuretics such as organic mercurials may be used with these drugs Ammonium chloride is most commonly prescribed but may irritate the stomach and cause nausea

Sedatives

Barbiturates For clinical purposes this group of drugs is usually divided into the short acting and the long acting groups The short acting drugs are not usually indicated in the treatment of heart disease except in unusual cases A confusingly large number of the long acting groups is available such as phenobarbital barbital neonal amytal ortal etc Perhaps the most satisfactory drug in the long acting group is phenobarbital which may be given in the form of tablets capsules suppositories or solution Usually it is prescribed in tablet form 0 1 Gm (1½ grains) being given at the hour of sleep In the elixir preparations the ordinary dosage is one teaspoonful three times a day Another long acting drug used frequently is amytal which may be given in tablet form 0 2 Gm (3 grains) being the usual dosage These preparations given in the above doses have little effect on the cardiovascular system although the blood pressure and pulse rate may fall as a result of the quieting action or sleep produced by their administration Untoward reactions may occur however when patients with congestive heart failure receive barbiturates Patients of the younger age group tolerate barbiturates better than those of the older group

Bromides For sedation of a mild degree bromides are employed frequently and tend to lessen anxiety and worry and to quiet patients with cardiac disorders or hypertensive vascular disease They are always given by mouth in the form of salts such as sodium potassium ammonium or calcium in capsules or in solution with syrupy vehicles They are usually given after meals and with plenty of water to disguise the unpleasant taste lessen gastric irritation and counteract the diuretic salt action of the various preparations Sodium bromide is perhaps the preferable drug but triple bromide which is a preparation containing equal parts of sodium potassium and ammonium salts of bromide prepared in effervescent salts is the most pleasant form in which to prescribe the drug Dosage of bromides cannot be stated dogmatically Moderate sedation is usually achieved

Diuresis usually occurs in one to 4 hours and is complete in 8 to 12 hours so it is best to give this drug in the morning It is usually given intravenously though it may be administered intramuscularly or rectally in suppository form but the latter is not recommended since it usually causes irritation It may also be given in tablet form once or twice a day preferably after a meal to avoid gastric irritation In patients with congestive heart failure and edema salyrgan decreases tubular reabsorption and outpouring of edema fluids

Mercupurin is a sodium salt of trimethylcyclopentane dicarboxylicacid methoxy mercury allylamide theophylline containing theophylline 3 5 per cent combined and 1 5 per cent free or 21 5 per cent mercury It differs from salyrgan in that camphoric acid is substituted for salicylic acid and is more effective and less toxic Mercupurin and salyrgan theophylline are given intravenously and intramuscularly mercupurin is usually given intramuscularly in patients with severe myocardial insufficency

Both mercuhydrin and mercuzanthin contain theophylline since it prevents necrosis of tissues at the site of injection increases the rate of absorption and prevents the storage of mercury These drugs may be given intramuscularly or intravenously thus promoting diuresis as to both quantity of urine excreted and duration of effect In some instances a slightly greater weight loss is seen when administered via the intramuscular route

The mercurials come in ampules containing 2 cc (30 minims) of a ten per cent solution of the drug and this is the intravenous or intramuscular dosage It is wise to give a smaller test dose of 0 5 cc (7½ minims) to see if there are any toxic effects Doses should be given every other day for several doses and then once a week if necessary A medication of acid forming salts should be administered if the mercurial alone does not produce the desired results Mercurials are especially indicated for cardiac edema and in patients with nephrotic edema but they should not be used in cases of nephritis Kidney damage and poisoning result from their use in cases of impaired renal function

The *acid forming salts* are composed of calcium chloride ammonium chloride and nitrate They exert an osmotic force in the tubular urine preventing water reabsorption and diuresis results These salts are given orally in either enteric-coated tablets or capsules in

When one administers the sulfonamides it is important to know the following When to use them which drug to employ the dosage how long to continue therapy, and what toxic reactions to watch for so proper treatment may be administered These drugs have not simplified but have complicated therapeutics Employment of them requires knowledge of the drug itself its absorption excretion distribution in the body and optimum blood level How it performs its beneficial action must be studied and most important of all for clinicians are the effects it has on the various systems of the body

The historical aspects of the development of sulfanilamide and its derivatives are interesting as well as instructive Without doubt Ehrlich must be given some credit for the development of the sulfanilamide preparations for it was he who studied the effect of dyes upon animals and parasites and bacterial organisms He dealt especially with the permeability of certain organisms to various kinds of dyes In 1908 a research chemist synthesized the chemical known as prontosil (diamino azo benzene sulfonamide) While this chemical was used in the composition of dyes its effect on disease was not considered important at that time In 1920 this formula for prontosil was patented in Germany It was not until 1933 that Foerster spoke of the use of prontosil in the treatment of staphylococcus infections In 1935 Domagk s stirring paper appeared He pointed out that prontosil was effective in controlling streptococcal infections in experimental animals in 100 per cent of cases Clinical reports attested the value of prontosil in medicine From 1936 until the present time there has been continuous activity in developing the various fields of sulfanilamide and its derivatives Sulfanilamide is the name applied in the United States for the chemical formula identical with the original prontosil of Germany The various sulfonamides are derivatives of the sulfanilamide nucleus

Mode of Action These drugs of the sulfonamide series have certain general features in common but the individual preparations possess specific therapeutic indications and are capable of selective toxic reactions

The aphorism of Ehrlich indicates his ideal in chemotherapy—a chemical agent which is maximally parasitotropic and minimally organotropic Some members of the sulfonamide group appear to come closer to this sought for ideal than others Yet it takes years of

in adults who are in good physical condition by administration of 1 to 3 Gm (15 to 45 grains) daily providing the patient is eating well This amount may prove toxic to some patients and the physician must be alert for the symptoms of bromide intoxication The drug should not be given for a period of over two or three weeks when patients cannot be kept under surveillance

Opiates The opiates should not be given when other drugs may be given to secure sedation tranquillity or sleep In many cases however the opiates must be resorted to in order to provide the necessary relief from insomnia restlessness or excitement and thus conserve the patients strength Morphine codeine papaverine and pantopon are the drugs most commonly used clinically

Chloral Hydrate This drug causes sedation usually without preliminary excitement Ordinarily it produces sleep in from 10 to 15 minutes after administration and is given in amounts of from 0 66 to 2 Gm (10 to 30 grains) It is ordinarily administered in water or milk or a syrupy vehicle Formerly it was believed that chloral hydrate had a depressing effect upon the heart muscle but this is largely erroneous the blood pressure may fall slightly from muscular inactivity Untoward cardiac effects occur only with toxic doses in patients with heart disease

The miscellaneous agents include paraldehyde sulfonal trianol etc and are not usually used in the treatment of heart disease

THE SULFONAMIDE DRUGS

There has been such an outpouring of literature on the sulfonamides during the past few years that one may assume a general knowledge of these drugs is possessed by all The chemical aspects the pharmacological action the therapeutic indications and the toxicological reactions of the sulfonamide drugs have been studied extensively To date the following members of the sulfonamide group have been established experimentally and clinically Sulfanilamide sulfapyridine sulfathiazole sulfadiazine sulfathaladine sulfasuxidine sulfamerazine and sulfaguanidine Most likely many other derivatives of the sulfanilamide nucleus will appear as time goes on for research workers and clinicians alike are striving for the model drug—one that hits the invading bacteria hardest and is least harmful to the body

neck sore throat peritonitis pneumonia or infection at any site Sulfapyridine has a special sphere of usefulness in pneumonia and in pneumococcal infections of the meninges the middle ear or elsewhere Sulfathiazole seems to be almost as good as sulfapyridine in the treatment of pneumonia and has a slight advantage in that it is less toxic Its special field of usefulness appears to be in its action against staphylococcal infections and pneumonia Sulfaguanidine is one of the newer preparations and its main action occurs in the large bowel The treatment of dysenteries particularly of the bacillary kind seems to be the special field for this drug

Sulfadiazine is the sulfonamide of choice in most infections with the exception of the streptococcal types where sulfanilamide remains the main drug Experiences with sulfadiazine in the treatment of pneumonia meningitis staphylococcal infections and to some extent streptococcal infections have been satisfactory It seems that sulfadiazine s superiority is accounted for by the fact that it passes with ease through membranes such as the meninges pleura and peritoneum The concentration of sulfadiazine in the spinal fluid can be raised to almost the same heights as that of the blood The chief reason for the popularity of sulfadiazine is its relative freedom from toxic reactions Vomiting and agranulocytosis occur infrequently Anemia is a rare complication Anuria hematuria and albuminuria are less common than with sulfapyridine but they must be watched for when sulfadiazine is used

Sulfamerazine is regarded clinically as the systemic sulfonamide of smaller dosage The advantage in the use of this drug lies in the fact that the dosage is approximately one half that of sulfadiazine or sulfathiazole Given orally it is more rapidly absorbed than the other sulfonamides resulting in a higher blood level in proportion to the dose It is particularly indicated in the treatment of beta hemolytic streptococcic infections and in pneumococcic infections such as pneumonia and otitis media

Dosages When indications appear which require the use of sulfonamide therapy the drug should be started promptly and repeated every three or four hours without interruption The initial dose of any one of the sulfonamides is about the same that is 2 to 4 Gm (30 to 60 grains) at once and 1 Gm (15 grains) every 4 hours with the exception of sulfamerazine which may be given every 6 to 8 hours

painstaking study to determine which drugs are most effective in controlling bacteria and at the same time are least toxic for the patient Not only the immediate toxic effects must be studied but also the remote consequences

The exact mode of action of the sulfonamides is not entirely known It is assumed that they have a bacteriostatic action and for practical purposes at this time it is a satisfactory explanation though a more precise action of the drug may be shown to exist later on Certain animals are more susceptible to the toxic effects of the sulfonamides than others dogs are especially resistant to them while guinea pigs rabbits and human beings are considerably less so The immediate toxic effects are well established but the consequences that may appear later are hardly known at all While all members of the sulfonamide drugs are used to treat almost any infection in the human being certain of them appear to be more effective in some infections and less active in others

Therapeutic Indications (Chart I) When confronted with a patient who has an infection one usually turns to the sulfonamide drugs for treatment It must be emphasized that the rules of therapeutics have not changed appreciably with the introduction of the sulfonamide drugs that is the best possible diagnosis should be made before applying the treatment The tendency to resort immediately to these powerful drugs is often followed with the best intentions of saving time and establishing treatment before it is too late It is doubtful if in most cases such haste is indicated or desirable But if a patient has an obscure infection of severe grade and the exact bacteriological diagnosis is not forthcoming within a reasonable length of time *e g*, 24 hours there should be *no* reluctance in giving one of these drugs without waiting for further reports As a rule a correct diagnosis from the bacteriological standpoint is desirable and important because the action of certain sulfonamides is more positive in some infections than in others

Sometimes there is confusion concerning which drug is to be chosen in a given case While an exact answer cannot be given to the question every time it is true that each of the drugs has a special field in which it appears to outdo the others in benefit to the patient For example sulfanilamide is the chief drug when a streptococcal infection is present whether it is an infection of the glands of the

It has been a practice to use citrocarbonate or sodium bicarbonate along with some of these preparations and there is a practical value in doing so Alkalinization seems to minimize the formation of sulfonamide crystals in the urinary tract One gram of sodium bicarbonate administered with each one gram of the sulfonamide will maintain an alkaline urine if fluid intake is adequate

Formerly it was believed that one had to be very careful about using other kinds of therapy along with the sulfonamide drugs because *toxic products might be formed This idea to a large degree* has been dispelled by more recent observations It probably is best not to use magnesium sulfate as a cathartic but usually even this procedure does not cause any trouble In using intravenous preparations glucose is not employed Plain distilled water is used because glucose with the drug forms a product which is not well absorbed by renal tubules and this renders it difficult to maintain average concentrations

Sometimes any one of the group causes nausea and vomiting and the drug must be discontinued by mouth When this occurs tincture of belladonna with elixir of phenobarbital may be given shortly before the administration of the drug and then it is borne better In case any of the sulfonamide drugs cannot be given by mouth for one reason or another it should be administered intravenously Sodium salts may be given in this way It is best to try to supplement the intravenous injections with as much of the drug as possible by mouth For intravenous use 5 Gm (75 grains) of the drug are dissolved in 100 cc of sterile distilled water and given two three or four times a day

In considering the therapeutic uses of any of the sulfonamide preparations it is important to remember that localized abscesses or collections of pus are not penetrated to any great extent by these drugs and therefore the usual methods of treatment surgical incision and drainage are indicated as in any other cases However vigorous treatment with the drugs may prevent the formation of such inaccessible collections of pus

Toxic Manifestation (Chart II) When one has decided to use a sulfonamide drug in treatment he must be willing to take on the responsibility of seeing that the patient is more benefited than harmed by the treatment This requires that he see the patient daily

until the disease is controlled The intestinal sulfonamide drugs require different dosage schedule (see Chart I) Naturally one wishes to build up the concentration of the drug in the blood stream to the optimal point as soon as possible and keep it there In certain individuals this is easy to do in others it is more difficult It is of considerable aid to determine the concentration of the drug in the blood stream every 2 to 3 days The absorption and excretion determine the concentration so it is necessary to know how much of the drug is in the blood stream for immediate action The quantity of fluid taken in a day has a direct influence on the concentration If 4000 or 5000 cc of fluid are administered daily the drug may be so diluted or washed out so rapidly that proper concentration in the blood is difficult to obtain The generally accepted procedure is to give the patient about 2500 cc of fluid a day which should yield about 1000 cc of urine

The optimal concentration runs about the same in all Between 8 and 12 mg per 100 cc with the exception of sulfathaladine sulfasuxidine and sulfaguanidine which are very slightly absorbed from the gastrointestinal tract

When the sulfonamides are used doses should be adequate Sometimes in a state of indecision one is apt to try a middle course and give small doses less often Experience shows that if the drug is injurious, a small dose will do about as much harm as a large one Therefore therapeutic doses should be given Occasionally there is hesitancy in giving the drug when the patient is very weak anemic jaundiced or when albuminuria is present These are not contraindications for the drug probably will not make these conditions worse When such features develop after one has been employing the drug for some time they may be signals that an essential organ is being damaged by the drug and of course then the drug must be stopped An error that creeps in occasionally in the management of patients is that the drug is stopped as soon as the patient shows a little improvement or when the fever drops to normal or near normal Continue to give the drug until the patient is well and afebrile for three or four days Otherwise the bacteria which have been rendered static and impotent for the time being may be replaced by more active forms and shortly one will see a recurrence of the same old symptoms of the disease

Sulfamerazine (4 methyl 2 ulfa nilamidopyrimi dine)	Pneumococcic pneumonia Hemolytic streptococcic infections Meningococcic meningitis	3 to 6 Gm depending on severity of illness	1 Gm every 8 hours
	Gonorrhea	1 5 Gm	1 5 Gm every 12 hours
Sulfasuxidine (Succinylsulfa thiazole) (2 (N succinylsulfanil amido) thiazole)	Preoperative preparation	0 25 Gm per Kg of body weight beginning 3 to 5 days before operation	0 25 Gm per Kg of body weight divided into 6 parts given every 4 hours
	Postoperative treatment	Continue same maintenance dose as before operation beginning as soon as patient can take an ounce of warm water without undue nausea	
	Bacillary dysentery Nonspecific diarrheas Ulcerative colitis Regional ileitis and ileojejunitis	0 25 Gm per Kg of body weight	0 25 Gm per Kg of body weight divided into 6 parts and given every 4 hours
	E coli infections of genitourinary tract	0 25 Gm of Kg of body weight in 4 or 6 divided doses for 1 week	0 125 Gm per Kg of body weight for from 1 to 2 weeks
Sulfathalidine (Phthalylsulfa thiazole) (2 (N[4] phthalylsulfanila mido) thiazole)	Ulcerative colit s Regional ileitis and ileojejunitis	0 1 Gm per Kg of body weight	0 1 Gm per Kg of body weight in 4 or 6 divided doses Reported effective also when given in dose of 3 Gm daily
	Preoperative treatment	0 125 Gm per Kg of body weight beginning 2 to 4 days before operation	0 125 Gm per Kg of body weight divided into 6 parts and given every 4 hours
	Postoperative treatment	Continue same dosage as before operation beginning as soon as patient can take an ounce of warm water without undue nausea	

Chart I — Sulfonamide Dosage Chart

Sulfonamide	Disease	Dosage: Initial Dose	Dosage: Daily Maintenance Dose
Sulfanilamide (*p* aminobenzene sulfonamide)	Severe infections	0.1 Gm per Kg of body weight	*Total daily dose of 0.1 Gm per Kg of body weight divided into 6 parts given every 4 hours day and night until temperature has been normal for 7 days*
	Mild and moderately severe infections	Total daily dose of 0.1 Gm per Kg of body weight divided into 6 parts and given every 4 hours day and night until temperature has been normal for 5 days	
Sulfathiazole 2 (*p* aminobenzene sulfonamido) thiazole	Pneumococcic pneumonia	4 Gm	1 Gm every 4 hours day and night until temperature has been normal 72 hours
	Gonorrhea	0.5 Gm every 3 hours for 6 doses on the first day of treatment	2 Gm per day for not more than 10 days If no improvement by 5th day shift to sulfapyridine Do not continue drug therapy more than 15 days
	Staphylococcic pneumonia	4 Gm	1 Gm every 4 hours day and night until temperature has been normal for 5 days If satisfactory results are not obtained increase daily dose by 25 to 50 per cent
	Staphylococcic cellulitis and lymphangitis	4 Gm	1.5 Gm every 4 hours day and night until infection is controlled Then 1 Gm every 4 hours day and night for 7 days
	Staphylococcic bacteremia	4 Gm	1.5 Gm every 4 hours until temperature has been normal for 48 hours then 1 Gm every 4 hours for an additional 2 weeks
Sulfadiazine 2 (*p* aminobenzene sulfonamido) pyrimidine	Pneumococcic pneumonia	0.1 Gm per Kg of body weight	1 Gm every 4 hours day and night until temperature has been normal for 3 days
	Mild or moderately severe hemolytic streptococcic infections	0.05 Gm per Kg of body weight	0.1 Gm per Kg of body weight divided into 6 parts given every 4 hours day and night until temperature has been normal for 5 days
	Gonorrhea	3 Gm	1 Gm every 6 hours for 5 days If blood count remains normal continue therapy for a total of not more than 8 days

for by simple clinical observations one can usually detect if the drug is not being tolerated well A blood count and urinalysis must be made at frequent intervals at least every second day so one can dis cover *the early evidences of an unfavorable effect upon the hemo* poietic system and the kidneys These are the safeguards that a pa tient may expect from the medical advisor The practice of giving *the drug and neglecting the patient is to be condemned A patient* may continue to take one of these preparations for a long time and no unfavorable complications may develop yet in another case a *serious result may occur when safeguards are overlooked*

There are certain toxic manifestations which are characteristic of the sulfonamide drugs as a group but some of the preparations have a *special tendency toward causing definite reactions In general* the group as a whole may affect the gastrointestinal organs the nervous system the hemopoietic organs and the renal system Nausea vomit ing and diarrhea are features of gastrointestinal intoxication The nervous system may become involved in more than one manner There may be actual peripheral neuritis but headache and mental depression are commoner Anemia agranulocytosis and purpura may occur with any of the drugs but particularly with sulfapyridine and sulfathiazole Hematuria and calcareous deposits in the kidneys do not occur with sulfanilamide but they are often present when sulfapyridine sulfathiazole or sulfadiazine are given

Sulfanilamide has a tendency to destroy the red blood cells and anemia is one of its characteristic toxic reactions Very little evi dence has been shown to the effect that sulfanilamide injures the kidneys *It* rarely causes agranulocytosis and hardly ever produces a fever or a rash Nausea and vomiting of course are features of all members of the sulfonamide group even sulfanilamide may occa sionally *cause these effects Headache and mental depression are also* features of sulfonamide intoxication

Sulfapyridine tends to cause agranulocytosis but not anemia Renal irritation is another of the toxic effects of this drug Sulfa thiazole has about the same characteristics as sulfapyridine but the rash and fever of sulfathiazole are almost specific features of its intoxi cation Sulfadiazine is peculiarly free from toxic manifestations Any of the reactions seen with the other drugs may occur with sulfadiazine but they hardly ever do Renal complications have been observed

Chart II — Toxic Effects of Sulfonamide Drugs

Toxic Manifestations	*Sulfanilamide*	*Sulfapyridine*	*Sulfathiazole*	*Sulfadiazine and Sulfamerazine*
Nausea and vomiting	Uncommon occurs early	Very frequent	Rare	Rare
Cyanosis	Common early and late	Faint common occurs early	Uncommon occurs early	Rare
Fever	Common 5th to 9th day may occur 1st to 21st day	Uncommon 5th to 9th day may occur 1st to 30th day	Common 5th to 9th day	*Seldom*
Rash	Common any form 5th to *9th day may occur 1st to* 21st day	Not common 5th to 9th day may occur 1st to 30th day	Common 5th to 9th day	Mild and rare
Kidney injury	Questionable	Common 1st to 10th day	Common 1st to 10th day	Common
Anuria with azotemia	Rare	Not uncommon 2nd to 14th day Blood pressure and fundi normal	Reported 7th day	Rare
Acute leukopenia with granulocytopenia	Not uncommon 1st to 10th day	Common especially in children 1st to 10th day	May occur 3rd to 10th day	Less than 2 per cent
Acute hemolytic anemia	Common especially in Negroes 1st to 5th day	Uncommon 1st to 5th day	Not reported	Rare
Stomatitis	Rare	Not reported	Not reported	None
Gastrointestinal tract	Bleeding rare diarrhea common	Bleeding reported	Not reported	Very little

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The toxic effects of sulfamerazine are very similar to those of sulfadiazine although nausea vomiting dizziness and headache occur less frequently than with the use of other sulfonamides

When general toxic reactions to the sulfonamides appear, the following treatment is instituted

1 The drug is discontinued until the toxic reaction clears up

2 When vomiting is the chief reaction the drug may be given intravenously in five per cent solution

3 If hemolytic anemia occurs transfusions and injections of liver extract intramuscularly are necessary

Injury to the kidney is the most frequent and serious toxic manifestation in sulfonamide therapy The two types of reaction are (1) Mechanical complications produced by masses of sulfonamide crystals in the kidneys pelves and ureters and (2) toxic intrarenal lesions occurring within the kidney but without mechanical obstruction The chief evidences of kidney damage include oliguria anuria and albuminuria Microscopic hematuria pus cells and granular casts are common Treatment of toxic reactions is now adequate and prevention of such reactions is steadily increasing Treatment includes the following

1 The drug is discontinued when evidence of damage is present

2 Fluids are given orally and or intravenously to augment excretion of the drug

3 Alkalinization by sodium bicarbonate orally or intravenously maintains the *p*H of urine at seven or above

4 Catheterization and lavage cleanse ureters and pelves

Alkalinization and maintenance of proper fluid intake and output during sulfonamide therapy keep toxic reactions and kidney impairment at a minimum

ABUSES OF THYROID THERAPY

Thyroid substitution therapy is one of the most reliable types of endocrine treatment but certain therapeutic hazards must be taken into consideration as well as opportunities of doing good

Excessive amounts of thyroid given to a patient for therapeutic purposes may bring on hyperthyroidism This kind of hyperthyroidism can sometimes be controlled by discontinuing thyroid ther

apy but at other times stopping the treatment does not regulate the condition and thyroidectomy may be necessary

In myxedema care must be taken lest certain organs be overtaxed This is particularly important when treating older patients There is danger of causing acute pulmonary edema coronary thrombosis or dilatation of the heart with left sided failure Too much thyroid may also produce shock of the addisonian type Diuresis may occur

The dosage varies with different people though young patients can tolerate as much as 0 26 Gm (4 grains) a day such doses are not recommended for all Thirty three milligrams (½ grain) a day will in a month bring metabolism up to –35 0 066 Gm (1 grain) to –25 0 13 Gm (2 grains) to –15 and 0 2 Gm (3 grains) to –10 One usually starts with 0 033 Gm (½ grain) for ten days and elevates the dosage each week as required Some patients may not be able to reach a normal level as their hearts will not stand the thyroid without developing cardiac failure or angina pectoris In cretins great care must be taken with the dosage as the margin between an inadequate dose and one large enough to produce untoward mental symptoms is small In women thyroid may cause menstrual scantiness or irregularities but it can correct menorrhagia

In addition to the symptoms cited thyroid can produce maniacal attacks echolalia diarrhea palpitation restlessness cardiac arrhythmias and fibrillations

In conclusion it is well to remember that all the endocrines are in balance A change in the thyroid balance alters that of the other glands Though some of the symptoms of overdosage are merely troublesome as are diarrhea or excessive sweating others as heart failure or shock may cause death

THERAPEUTIC HAZARDS OF BENZEDRINE

Benzedrine is a sympathomimetic amide resembling ephedrine except that it possesses greater ability to stimulate the higher centers particularly the cortex

The indiscriminate use of benzedrine may cause toxic effects varying with the individual Cerebral symptoms are the outstanding toxic effect The drug may cause restlessness tremors insomnia talkativeness irritability confusion assaultiveness hallucinations delirium panic states or homicidal or suicidal intentions Such central stimu

lation may be followed by fatigue and depression Gastrointestinal disturbances such as dry mouth metallic taste anorexia nausea vomiting and diarrhea have been known to occur The cardiovascular reactions are chilliness sweating palpitation marked hypertension or hypotension extrasystoles anginal pain circulatory collapse and syncope

Prolonged inhalations according to Waud may result in hypertension lasting for days anorexia loss of weight, mental stimulation followed by fatigue and depression Permanent organic changes do not often occur The inference is that benzedrine is a safe drug for normal persons However severe reactions including coma clonic convulsions and panic have been recorded Smith told of a case of death possibly due to benzedrine

Benzedrine should not be used to overcome sleepiness or to increase the energy It is contraindicated for persons with hypertension advanced arteriosclerosis coronary artery disease states of mental excitement agitated depression or hyperthyroidism It should be used cautiously in those with anorexia insomnia vasomotor instability, asthenia psychopathic personalities or suicidal tendencies Habituation similar to that of nicotine and caffeine may develop but addiction is unknown Some patients report increased tolerance after continued use of the drug but change in susceptibility does not occur as a rule in most people

CHAPTER XXV

Penicillin

In 1929 Professor Alexander Fleming gave the name penicillin to a bacterio inhibitory agent produced by a strain of mold of the *Penicillium notatum* Fleming saw the advantages of penicillin over the chemical antiseptics then in use and he suggested that penicillin might be an efficient antiseptic for application to or injection into areas infected with penicillin sensitive microbes

Today although strictly speaking it is not an antiseptic these properties of an ideal antiseptic are recognized in penicillin (1) It possesses enormous bacteriostatic power and the number of bacteria present does not affect its action to a noticeable extent (2) it acts effectively in almost any medium Blood serum and pus do not inhibit its power (3) it is almost completely nontoxic to the body as a whole and to the organs of the body (4) it is soluble in a number of substances normal saline solution distilled water and five per cent dextrose and it is also effective in powder and cream form (5) it may be administered in several ways intravenously intramuscularly topically intrathecally orally and locally depending upon the type and severity of the infection

Since penicillin is an unstable substance it is combined therapeutically with sodium barium and calcium although sodium salt of penicillin is most commonly used

Indications Penicillin is bacteriostatic and it has been suggested that the action of the drug may be on bacterial fission since it is most effective when multiplication of bacteria takes place With the exception of the gonococcus and meningococcus susceptible bacteria are almost all Gram positive

The diseases which are known to respond to penicillin recommended in a report by Dr C S Keefer Chairman of the Committee on Chemotherapy of the National Research Council and his Associates are the following

Penicillin is the best therapeutic agent in the treatment of

1 All staphylococcic infections with and without bacteremia This includes acute osteomyelitis carbuncles—soft tissue abscesses meningitis

pneumonia—empyema cavernous or lateral sinus thrombosis car buncle of kidney and wound infections
2 All cases of clostridia infections
3 All hemolytic streptococcic infections with bacteremia and all serious local infections This includes cellulitis mastoiditis and its complica tions pneumonia and empyema puerperal sepsis peritonitis
4 All anaerobic streptococcic infections
5 All pneumococcic infections of meninges pleura and endocardium and all cases of sulfonamide resistant pneumococcic pneumonia
6 All gonococcic infections complicated by arthritis ophthalmia endo carditis peritonitis epididymitis and all cases of sulfonamide resistant gonorrhea

Penicillin has also been found to be an effective agent in syphilis actinomy cosis and bacterial endocarditis but its position has not been definitely defined

Penicillin is of questionable value in mixed infections of the peritoneum and liver in which the predominating organism is of the gram negative flora This includes ruptured appendix liver abscesses and urinary tract infections

All gram negative bacillary infections constitute a contraindica tion for penicillin It is also ineffective in the treatment of tubercu losis rheumatic fever Hodgkin s disease leukemia poliomyelitis virus infections and cancer

These indications and contraindications cannot in any sense be considered the final statement on penicillin therapy Much research work is being done at the present time and will be done in the future on this drug its indications dosages methods of administration and its usefulness in combination with other sub stances There is no doubt but that even more successful results will follow a more inclusive field of therapy

Dosage The dosage varies with the type and severity of the infection The age weight and general condition of the patient are also taken into account Exact dosage for many infections and diseases is not known but enough penicillin must be given to pre vent the growth of the infecting organisms The antibacterial action parallels the concentration of penicillin in the blood While an overdose has not been proved harmful an underdose may result in therapeutic failure and possible death To determine whether an adequate amount of penicillin is being given the blood is titrated and the concentration of the drug determined The entire clinical

response of the patient is determined by the temperature pulse disappearance of pain negative results of blood or urine cultures and general improvement

Recently simplified dosage schedules have come into use All routine cases of acute and chronic infection receive 120 000 to 240 000 units per day Better results are obtained if larger daily doses are given over a longer period of time Dosage is continued for about a week after the infection subsides and the temperature returns to normal During this time there is also a marked improvement in the general mental and physical condition of the patient If however there is no response to therapy after 48 hours the dosage is increased

Methods of Administration Here again the type of administration depends upon the type of infection present C S Keefer and his associates recommended the following methods of administration Serious infections due to the hemolytic streptococcus staphylococcus or pneumococcus are best treated by constant or frequent intravenous injections chronically infected compound injuries by parenteral injection plus local treatment sulfonamide resistant gonorrhea by intravenous or intramuscular injection empyema, by injection into the empyema cavity after aspiration of pus or fluid meningitis by injection into the subarachnoid space or intracisternally in conjunction with systemic administration

It is essential that penicillin be given as early and as promptly as possible in the treatment of acute infections It is advisable in these cases to give penicillin intravenously or intramuscularly by the continuous drip method for the first three or four days to maintain the concentration of penicillin in the blood at 0 5 units per cc Afterwards intramuscular injections at intervals of two to four hours may be given As stated above the dosage schedule varies but 30 000 units every three hours intramuscularly is the usual amount given

It is not easy to decide when to discontinue treatment for several factors must be given thorough consideration It is wise though to continue treatment in somewhat reduced dosage for a week or ten days after the temperature becomes normal and the patient seems quite well In subacute bacterial endocarditis for example active treatment is continued for six weeks or longer then penicillin is given by mouth for another month or so

Intravenous administration of the drug may be continuous or intermittent Continuous infusion of penicillin maintains a constant therapeutic level in the blood The standard solution consists of 100 000 units of penicillin dissolved in 1000 cc of physiological saline When therapy is initiated 100 or 200 cc are given rapidly and then the rate is regulated to 30 or 40 drops per minute Disadvantages lie in the difficulty of continuous infusion the possible discomfort of the patient and the frequent occurrence of superficial venous thrombosis However this is the preferred method if the infection is serious and if the time element is important Intermittent intravenous administration is given every three hours to maintain a therapeutic level The interval between doses cannot safely be prolonged because of the rapid fall in blood concentration and the rapid urinary excretion

Intramuscular administrations are best given in the gluteus maximus or deltoid muscle A higher concentration of penicillin is maintained for a longer period of time in intramuscular than in intermittent intravenous administration and injections are given at three or four hour intervals These injections are given more easily and may be better tolerated especially by patients who cannot take the amount of fluid necessary for continuous intravenous infusion In addition after the danger of severe infection is past equal intramuscular injections may replace intravenous therapy A change in the vehicle in which the penicillin is administered will usually relieve any discomfort on injection but it is important to keep the volume of fluid as low as possible 5000 units per cc of fluid and to change the site of injection to prevent or minimize discomfort

Following subcutaneous injection the absorption of penicillin is decidedly delayed and the concentration of the drug in the blood does not reach the levels obtained in the methods of administration discussed above

Intrathecal injection has been successfully used in conjunction with intravenous or intramuscular injections in the treatment of meningitis Not more than 20 000 units in 10 cc of isotonic sodium chloride solution injected once or twice daily is recommended

Local application of penicillin calls for comparatively small amounts It has proved successful in pleural and joint infections

wounds burns and scalds The drug may be used locally in powder form diluted with a powder of one of the sulfonamide compounds in cream form or in a solution of isotonic sodium chloride In wounds and infections which require constant therapy wet dressings are applied In infections of the extremities frequent immersions in penicillin solution are helpful In deep wounds continuous instillations or frequent injections are valuable Care must be taken to assure adequate access of the drug to all parts of the infection or wound

Injection of penicillin has been made into the pleura pericardium joints bone marrow and subarachnoid space either alone or in combination with other penicillin therapy and excellent results have been obtained because the drug is absorbed slowly

Oral penicillin is now available in several forms Usually each tablet or capsule contains 25 000 to 50 000 units The advantages of oral penicillin over other forms of administration are quite apparent if the end results are comparable It is becoming established that the penicillin level of the blood may be maintained by the oral method as well as by the other methods of administration although the doses must be somewhat larger The average dose of oral penicillin is from 200 000 to 300 000 units a day Penicillin may be given by injection during the acute phase of a disease and after the infection is under control oral penicillin may be substituted

The quantity of penicillin excreted in the urine depends upon the route of administration the amount given and the urinary output However excretion averages between 50 and 60 per cent of the amount of the drug given It has been proved that renal suppression decreases the amount of the drug excreted in the urine If the urinary output could be controlled the need for large and frequent doses of the drug might be done away with Excretion of penicillin by other routes has not been completely studied but thus far none has been recovered from saliva tears or spinal fluid and the fate of approximately 40 per cent of the drug remains undetermined

Penicillin as a Prophylactic Measure The value of penicillin as a prophylactic measure is receiving more serious attention than ever before It is generally believed that the intramuscular injection of 25 000 units every 4 hours for two or three days is a satisfactory

therapeutic measure when a patient is threatened with a serious infection It is highly probable that 25 000 to 30 000 units by mouth every two hours for several days may be an adequate measure in the prevention of the less serious infections Kolmer states that penicillin may be of prophylactic value in the prevention of the following disorders (1) Infections of war and other traumatic and postoperative wounds (2) infections of compound fractures (3) septicemia in acute and chronic osteomyelitis (4) empyema following lobectomy or pneumonectomy (5) puerperal endometritis following abortion miscarriage or difficult labor (6) gas gangrene following amputations (7) peritonitis due to infections following rupture of an appendix *or open wounds of the intestines (8) staphylococcal and strepto*coccal infections (9) lateral sinus thrombosis and meningitis due to extension of infections from the mastoids or nasal accessory sinuses *particularly after operation (10) infection in eye injuries*

Toxic Reactions Normally penicillin is nontoxic in doses far exceeding those given in treatment and the majority of toxic reactions are thought to be caused by impurities or adulterants As it is now used clinically penicillin contains from 10 to 51 per cent pure penicillin the toxicity is low and systemic reaction is infrequent *Reactions reported by G I Schmitt* attributable to the drug itself are (1) Urticaria (2) fever in afebrile patients (3) transient azotemia and (4) thrombophlebitis at the site of injection

Reactions which may be caused by impurities in the penicillin are (1) Chills with or without fever following intravenous injection (2) eosinophilia (3) burning pain at the site of intramuscular *injection (4) headache (5) faintness* and flushing (6) unpleasant taste following parenteral injection (7) tingling in testes (8) muscle cramps (9) femoral phlebothrombosis

*Frequent comparisons of penicillin and the sulfonamide com*pounds have been made and the following advantages are possessed by penicillin (1) It is more powerful in its bacteriostatic action against *streptococci and staphylococci* (2) *its action is* minimally affected by the number of bacteria present (3) *it is not affected* by the medium in which it acts (4) it is essentially nontoxic even in large *doses However combined penicillin and sulfonamide* therapy is believed to be more effective than either drug alone in streptococcic and staphylococcic infections

A whole new field opens when the possibility of penicillin com bined with other drug therapy is considered Alexander Fleming believes the most important step for the future is the analysis and synthesis of penicillin, which may lead to a series of new prepara tions having wider application than penicillin itself

Current Penicillin Problems While it is a well accepted fact that penicillin is of inestimable value in the treatment of many acute in fections much recent work has stressed two of its shortcomings Its rapid excretion and the possible development of resistant strains

Penicillin is excreted so rapidly that frequent (3 hourly) par enteral injections becomes a necessity if an adequate blood level is to be maintained Attempts have been made to delay the absorption from local deposits in the muscles by creating a depot of penicillin from which it is slowly absorbed Solutions in beeswax peanut oil and other oil substances have been used but have been unpopular because they are difficult to inject they are not without local dis comfort and their efficacy is doubtful However they are becoming more widely used and accepted by many authorities More promis ing measures are those which delay excretion of penicillin by control of tubular excretion since about 80 per cent of the drug is filtered through the tubules Recent experiments indicate that caronamide 2 to 3 Gm every 4 hours has appeared to block the specific enzyme transport system responsible for the passage of penicillin through the tubular epithelium and with simultaneous use of penicillin raises the blood level two to seven times

The development of penicillin resistant strains includes the pos sibility of mutation of sensitive into resistant organisms and the foster ing of the growth of nonsensitive organisms of the same or other strains

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NOTE Names of therapeutic agents and procedures are set in *italics* Page numbers in *italics* refer to illustrations The abbreviation *vs* (versus) indicates differentiation

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